



Delayed neuromuscular recovery after use of sugammadex in a patient with amyotrophic lateral sclerosis: a case report

Tsong-Bih Chang, Jin Huh

ABSTRACT

Department of Anesthesiology and Pain Medicine, Kangwon National University Hospital, Kangwon National University School of Medicine, Chuncheon, Republic of Korea

Correspondence: Jin Huh, Department of Anaesthesiology and Pain Medicine, Kangwon National University Hospital, Kangwon National University School of Medicine, 156 Baengnyeong-Ro, Chuncheon, Gangwon-Do 200-722, Republic of Korea; Tel: +82-33-258-2315; Fax: +82-33-258-2459; E-mail: huhjin419@gmail.com

Received : 25 May 2017
Reviewed : 30 May 2017
Corrected & Accepted : 30 May 2017

This case report describes delayed muscular recovery in a patient with amyotrophic lateral sclerosis (ALS) after general anesthesia using rocuronium and sugammadex. A 62-year-old woman with ALS with bulbar involvement underwent ureteroscopic ureterolithotomy. We performed standard general anesthesia using propofol, rocuronium and sevoflurane with standard and neuromuscular monitoring. Rocuronium was administered at a dose of 20 mg (0.38 mg/kg) to facilitate endotracheal intubation, and anesthesia was maintained with sevoflurane in the range of 1-3 vol%. After the procedure, 100 mg of sugammadex (1.92 mg/kg) was administered and a train-of-four (TOF) ratio > 0.9 was observed in 80 s. However, the muscle strength was not the same as the preoperative level and tidal volume was judged to be inadequate for extubation. No further improvement in muscle strength was observed after administration of an additional 100 mg of sugammadex. The patient was transferred to the intensive care unit and pressure support ventilation was applied. Muscle strength was checked periodically and tracheal extubation was performed based on complete neuromuscular recovery to preanesthetic level after 4 h.

Key words: Amyotrophic lateral sclerosis; Sugammadex; Train-of-Four

Citation: Chang TB, Huh J. Delayed neuromuscular recovery after use of sugammadex in a patient with amyotrophic lateral sclerosis: a case report. *Anaesth Pain & Intensive Care* 2017;21(4):475-478

INTRODUCTION

Amyotrophic lateral sclerosis (ALS) is a disease characterized by the progressive degeneration of upper and lower motor neurons in the motor cortex, brainstem, and spinal cord.¹ The clinical features of ALS include progressive muscle weakness, respiratory insufficiency, spasticity, hyperreflexia, and bulbar symptoms, such as dysarthria and dysphagia.^{2,3} ALS patients show increased susceptibility to neuromuscular blockers (NMBs), and neuromuscular monitoring is an indispensable part of general anesthesia (GA) in such cases.⁴ However, in recent reports, the objective results obtained by neuromuscular monitoring are sometimes inconsistent with clinical findings in

ALS patients.^{4,5} Sugammadex reverses any degree of rocuronium- or vecuronium-induced blockade by encapsulating, and thereby inactivating the NMBs.^{6,7} There have been several clinical reports regarding the successful management of ALS patients using rocuronium-sugammadex under neuromuscular monitoring for GA.^{4,5,8}

Here, we report a case of delayed neuromuscular recovery after reversal of rocuronium-induced neuromuscular block with sugammadex and train-of-four (TOF) ratio reaching > 0.9 in a patient with ALS.

CASE REPORT

A 62-year-old woman (height 167 cm; weight 52 kg)

Delayed recovery with sugammadex in ALS

was scheduled for ureteroscopic ureterolithotomy. The patient's medical history included a diagnosis of ALS 3 years previously and she had problems in speaking and swallowing solid food due to bulbar muscle involvement. Preoperative neurological examination showed aphonia, aphasia, grade 1/5 motor power in all extremities, hypoactive pharyngeal reflex, and enhanced deep tendon reflexes. Preoperative complete blood count, biochemistry values, chest x-ray, and ECG trace were normal. Based on preoperative discussion with a urologist, GA was planned considering the possibility of conversion to laparoscopic ureterolithotomy.

The patient was not premedicated, and standard monitoring devices were applied upon arrival in the operating room. GA was induced with 80 mg of propofol, and neuromuscular block monitoring was started using repetitive TOF stimulation (TOF-Watch SX; Organon, Dublin, Ireland) on the ulnar nerve. The baseline values of TOF ratio were > 0.90. A single dose of rocuronium (20 mg), titrated in increments of 10 mg to a TOF count of 0, was administered intravenously to facilitate tracheal intubation. After uneventful tracheal intubation, the patient was placed in the lithotomy position and anesthesia was maintained with sevoflurane 2% in a mixture of 50% oxygen in air. Peripheral skin temperature was maintained above 34°C using a forced air warming device. During the operation, no additional NMBs were used and all hemodynamic parameters were within normal limits. The operation was completed uneventfully and the total anesthesia time was 84 min. At the end of surgery, all anesthetic medications were stopped and the TOF ratio was 0.65. We administered 100 mg of sugammadex intravenously and monitored TOF ratio. About 80 s later, the ratio was > 0.90 and the patient could respond to verbal commands by blinking her eyes. Although the patient was breathing spontaneously, the tidal volume was inadequate and muscle strength was reduced than the preoperative level. Accordingly, an additional 100 mg of sugammadex was given for complete reversal of neuromuscular block. After 30 min of observation, no further improvement in muscle strength was observed; therefore, the patient was transferred to the intensive care unit and pressure support ventilation was applied.

In the intensive care unit, the muscle strength and respiratory parameters were checked periodically and tracheal extubation was done based on complete neuromuscular recovery to the preanesthetic level 4 h later. Arterial blood gases, electrolytes, and other biochemistry parameters were within normal limits

following extubation. The patient remained in the intensive care unit with close monitoring for 1 day and was then transferred to the general ward.

DISCUSSION

Appropriate reversal of neuromuscular blockade is essential to avoid adverse outcomes, especially in patients with neuromuscular disorders. Patients with ALS show increased sensitivity to non-depolarizing NMBs.⁴ Therefore, complete recovery of muscle strength should be present, and the residual effect of NMBs should be fully reversed pharmacologically or ensured to recover spontaneously. Previously, anesthetic management of patients with ALS using NMBs represented a major challenge to anesthesiologists. However, after the introduction of sugammadex, this agent was reported to successfully reverse the neuromuscular blocking effects of non-depolarizing NMBs; the combination of rocuronium and sugammadex should be considered, whenever there is an indication for neuromuscular block in patient with ALS.^{4,5,8}

In our case, we administered a small amount of rocuronium (0.38 mg/kg) and attempted to reverse its effect by sugammadex. Following administration of sugammadex, the TOF ratio was > 0.9 and the patient was able to breathe spontaneously. A TOF ratio of 0.9 is regarded as a reasonable indicator to exclude postoperative residual paralysis.⁹ However, in our patient, the range of motion and muscle strength were not fully restored to the preanesthetic levels. Considering the total amount of sugammadex (3.85 mg/kg)¹⁰ used to reverse the effect of rocuronium and the TOF ratio, these were incompatible with the clinical findings in our patient. One possible explanation for this phenomenon may be the residual muscle relaxation effect of sevoflurane. Inhaled anesthetics have muscle relaxation properties by themselves and also potentiate the action of NMBs.¹¹ Although the specific sites of action of inhaled anesthetics on motor pathways are not fully known, various areas from the cerebral cortex to skeletal muscle have been reported as sites of action in addition to neuromuscular junctions.¹²⁻¹⁴ The effects of inhaled anesthetics on these sites other than neuromuscular junctions - the main sites of action of NMBs, could not be reflected by the TOF test. In general, these effects of inhaled anesthetics are negligible when complete reversal of the effects of NMBs by sugammadex or cholinesterase inhibitor was attained in patients with mild neuromuscular disorders. There have been several reports of the successful use of sugammadex for neuromuscular block reversal in patients with ALS.^{4,8} In our case,

ALS was in a progressed state, with bulbar symptoms and weakness involving most of the skeletal muscles. Therefore, inhaled anesthetics may have a clinically significant effect on recovery from neuromuscular paralysis.

Previous case reports in ALS patients have also shown discrepancies between the TOF response (> 0.9) and clinical findings in relation to muscle recovery during anesthetic emergence.^{4,5} In these cases, however, extubation was performed successfully without any complications after the use of sugammadex (1-2 mg/kg). This difference from our experience may also be explained in part by the degree of disease progression and the muscle relaxation effect of inhaled anesthetics. However, there have been insufficient investigations and case reports providing detailed information about the role of sugammadex and interpretation of TOF responses according to progression of ALS. Considering previous reports and ours, TOF > 0.9 may not be used as the absolute criteria for safe extubation and full recovery from muscle paralysis in ALS patients.

Regional anesthesia could be a viable option for anesthetic management of ALS patients in cases in which surgery does not require deep muscle paralysis or is confined to the extremities. Various regional anesthetic techniques rather than general inhalation anesthesia have been used successfully in the anesthetic management of ALS patients.^{15,16} However, the possibilities of neurological insult and exacerbation of ALS progression should be taken into consideration.¹⁷ If the operation involves areas of the torso, as in our case, regional anesthesia would not be applicable and GA should be considered. Xiao et al.¹⁸ reported the successful use of total intravenous anesthesia (TIVA) without muscle relaxant in a parturient with ALS. Compared with inhaled anesthetics, propofol is known to have no marked influence on neuromuscular function.¹⁸ Remifentanyl, an ultrashort-acting opioid, is regarded

as a safe analgesic drug for continuous infusion with little disturbance of postoperative respiratory function. With regard to these pharmacological properties of propofol and remifentanyl, TIVA without muscle relaxation may be a better anesthetic option than general inhalation anesthesia in ALS patients; however, it is unclear whether TIVA is better for anesthetic management of patients with advanced ALS. Further studies are therefore needed to clarify whether TIVA is indeed superior to inhalation anesthesia in such cases.

CONCLUSION

Complete recovery from muscle paralysis to the preanesthetic level was challenging in the general anesthetic management of our ALS patient. Although sugammadex is very efficient for the reversal of rocuronium-induced neuromuscular block in inhalation GA, the use of sugammadex and TOF ratio > 0.9 do not always guarantee the avoidance of postoperative residual paralysis in patients with advanced ALS with severe muscle weakness. In conclusion, clinical findings indicating the recovery of muscle paralysis should be considered carefully in addition to objective data from neuromuscular monitoring devices in the anesthetic management of ALS patients. Total intravenous anesthesia using potent ultrashort acting narcotics without neuromuscular blocking agents may be preferred in selected patients.

Conflict of interest: The authors had no conflicts of interest to declare in relation to this article.

Funding/Support: This study was supported by 2016 Research Grant from Kangwon National University (No. 520160282).

Authors' Contribution: All of the authors took part in management of the case and the manuscript preparation.

[The English in this document has been checked by at least two professional editors, both native speakers of English. For a certificate, please see: <http://www.textcheck.com/certificate/k9Hg3R>]

REFERENCES

1. Chou SM, Norris FH. Amyotrophic lateral sclerosis: lower motor neuron disease spreading to upper motor neurons. *Muscle & nerve* 1993;16(8):864-9. [PubMed]
2. Tandan R, Bradley WG. Amyotrophic lateral sclerosis: Part 1. Clinical features, pathology, and ethical issues in management. *Annals of neurology* 1985;18(3):271-80. [PubMed] [Free full text]
3. Tandan R, Bradley WG. Amyotrophic lateral sclerosis: Part 2. Etiopathogenesis. *Annals of neurology* 1985;18(4):419-31. [PubMed]
4. Kelsaka E, Karakaya D, Zengin EC. Use of sugammadex in a patient with amyotrophic lateral sclerosis. *Med Princ Pract.* 2013;22(3):304-6. doi: 10.1159/000343168. [PubMed] [Free full text]
5. Chang YJ, Jung WS, Son WR, Jo YY. Discordance between train-of-four response and clinical symptoms in a patient with amyotrophic lateral sclerosis. *Acta medica Okayama* 2014;68(2):125-7. [PubMed] [Free full text]
6. Bom A, Bradley M, Cameron K, Clark JK, Van Egmond J, Feilden H, et al. A novel concept of reversing neuromuscular block: chemical encapsulation of rocuronium bromide by a cyclodextrin-based synthetic host. *Angew Chem Int Ed Engl.* 2002 Jan 18;41(2):266-70. [PubMed]
7. Puhlinger FK, Rex C, Sielenkamper AW, Claudius C, Larsen PB, Prins ME, et al. Reversal of profound, high-dose rocuronium-induced neuromuscular blockade by sugammadex at two different time points: an international, multicenter, randomized, dose-finding, safety assessor-blinded, phase II trial. *Anesthesiology* 2008;109(2):188-97. doi: 10.1097/ALN.0b013e31817f5bc7. [PubMed] [Free full text]
8. Wachi M, Uehara K, Fujinaka W, Takatori M, Tada K. [Use of sugammadex in a patient with amyotrophic lateral sclerosis]. *Masui. The Japanese journal of anesthesiology* 2011;60(12):1408-10. [PubMed]
9. Claudius C, Viby-Mogensen J. Acceleromyography for use in scientific and clinical practice: a systematic review of the evidence. *Anesthesiology* 2008;108(6):1117-40. doi: 10.1097/ALN.0b013e318173f62f. [PubMed] [Free full text]
10. Brull SJ, Kopman AF. Current Status of Neuromuscular Reversal and Monitoring: Challenges and Opportunities. *Anesthesiology* 2017;126(1):173-90. [PubMed] [Free full text]
11. Pereon Y, Bernard JM, Nguyen The Tich S, Genet R, Petitfaux F, Guiheneuc P. The effects of desflurane on the nervous system: from spinal cord to muscles. *Anesthesia and analgesia* 1999;89(2):490-5. [PubMed]
12. Woodforth IJ, Hicks RG, Crawford MR, Stephen JP, Burke D. Depression of I waves in corticospinal volleys by sevoflurane, thiopental, and propofol. *Anesthesia and analgesia* 1999;89(5):1182-7. [PubMed]
13. Thornton JA, Whelpton D, Borwn BH. The effect of general anaesthetic agents on nerve conduction velocities. *British journal of anaesthesia* 1968;40(8):583-7. [PubMed]
14. Rampil IJ, King BS. Volatile anesthetics depress spinal motor neurons. *Anesthesiology* 1996;85(1):129-34. [PubMed] [Free full text]
15. Arai Y, Yoshida T, Mizuno Y, Miyashita T, Goto T. [Epidural Anesthesia with Non-invasive Positive Pressure Ventilation for Laparotomy in a Patient with Amyotrophic Lateral Sclerosis]. *Masui.* 2015;64(10):1062-4. [PubMed]
16. Park KB, Son B, Hwang DY, Jeon Y. Spinal anesthetic management for discectomy in a patient with amyotrophic lateral sclerosis -A case report. *Korean J Anesthesiol.* 2012 Dec;63(6):547-9. doi: 10.4097/kjae.2012.63.6.547. [PubMed] [Free full text]
17. Vercauteren M, Heytens L. Anaesthetic considerations for patients with a pre-existing neurological deficit: are neuraxial techniques safe? *Acta anaesthesiologica Scandinavica* 2007;51(7):831-8.
18. Xiao W, Zhao L, Wang F, Sun H, Wang T, Zhao G. Total intravenous anesthesia without muscle relaxant in a parturient with amyotrophic lateral sclerosis undergoing cesarean section: A case report. *Journal of clinical anesthesia* 2017;36:107-09. [PubMed]

