

# The use of sugammadex in a patient with Kennedy's disease under general anesthesia

Risa Takeuchi,

Hiroshi Hoshijima<sup>1</sup>,

Katsushi Doi<sup>2</sup>, Hiroshi Nagasaka

Departments of Anesthesiology, Saitama Medical University Hospital, Saitama, <sup>2</sup>National Hospital Organization Hamada Medical Center, Shimane, <sup>1</sup>Departments of Dento-oral Anesthesiology, Tohoku University Graduate School of Dentistry, Sendai, Japan

## Address for correspondence:

Dr. Hiroshi Hoshijima,  
Departments of Dento-oral  
Anesthesiology, Tohoku University  
Graduate School of Dentistry,  
4-1 Seiryomachi, Aoba-ku,  
Sendai 980-8575, Japan.  
E-mail: hhoshi6@gmail.com

## ABSTRACT

Kennedy's disease (KD), also known as spinal and bulbar muscular atrophy, is a rare, X-linked recessive, neurodegenerative disorder of the lower motor neurons characterized by progressive bulbar and appendicle muscular atrophy. Here we report a case of a 62-year-old male patient with KD, weighing 70 kg and 173 cm tall, was scheduled for frontal sinusectomy due to sinusitis. General anesthesia was induced through propofol 80 mg, remifentanyl 0.25 µg/kg/min and 40 mg rocuronium. We were successfully able to use a sugammadex on a patient suffering from KD in order to reverse rocuronium-induced neuromuscular blockade.

**Key words:** *Kennedy's disease, sugammadex, general anesthesia*

## INTRODUCTION

Kennedy's disease (KD), also known as spinal and bulbar muscular atrophy, is a rare, X-linked recessive, neurodegenerative disorder of the lower motor neurons characterized by progressive bulbar and appendicle muscular atrophy.<sup>[1-3]</sup> KD has several important features that must be taken into consideration by Anesthesiologists. Spontaneous but self-limited laryngospasms occur with increased frequency in this patient population;<sup>[3,4]</sup> it is unknown if these patients are at increased risk of laryngospasm with airway manipulation during anesthesia. These patients can be debilitated when in the later stages of the disease and may have profound bulbar dysfunction with a theoretical increase in the risk of aspiration.<sup>[1]</sup> Given the motor neuron involvement in KD, the safety of muscle relaxants has not been established.

Although a cases series of anesthetic reports on the general anesthetic management of patients with KD has been published,<sup>[5]</sup> the use of rocuronium and sugammadex have not yet been reported. Sugammadex, a newly introduced modified l-cyclodextrin, encapsulates steroidal neuromuscular blocking drugs and may therefore reverse rocuronium-induced neuromuscular block. We report the successful use of sugammadex to reverse a rocuronium-induced neuromuscular block in a patient with KD.

## CASE REPORT

The present case report is about a 62-year-old male patient with KD, weighing 70 kg and 173 cm tall, was scheduled for frontal sinusectomy due to sinusitis. He first noticed muscle weakness in the proximal part of the lower limbs at the age of 43. At 2 years later, he was diagnosed with KD. Pre-operative physical examination revealed muscular atrophy, weakness and fasciculation in the lower upper limb muscles and diminished deep tendon reflexes in the lower and upper extremities. He had slurred speech and slight difficulties in swallowing. Other findings included fasciculation and atrophy of the tongue and facial muscles, but he had not experienced laryngospasms [Figure 1]. Pre-operative blood tests were within the normal range except for a plasma creatine kinase concentration of 335 µl

### Access this article online

Quick Response Code:



Website:

www.saudija.org

DOI:

10.4103/1658-354X.136640



**Figure 1:** Atrophy of tongue

(normal range: 24-195  $\mu$ l). His older brother had died as a result of KD 2 years earlier.

The patient was not premedicated and was monitored with electrocardiography, noninvasive blood pressure and pulse oximetry. Following pre-oxygenation, general anesthesia was induced via propofol 80 mg and remifentanyl 0.25  $\mu$ g/kg/h. After the loss of consciousness, neuromuscular monitoring was applied and calibrated using objective evoked electromyography of the adductor pollicis muscle using an NS-272 neuromuscular transmission nerve stimulator (Fisher and Paykel Health care Ltd., New Zealand). The left or right ulnar nerve was stimulated at the wrist with supramaximal and square-wave stimuli of 0.2 ms duration, 2 Hz every 15 s. The fade was not detected before the administration of rocuronium.

After induced anesthesia, train of four (TOF) ratios was indicated 1.0. We then administered 40 mg rocuronium boluses and deep neuromuscular blockade was achieved ( $T_4/T_1 = 0.0$ ) after 120 s. We performed the tracheal intubation without any complications. Anesthesia was maintained uneventfully with 5-8 mg/kg/h propofol and remifentanyl 0.2-0.25  $\mu$ g/kg/min in oxygen and air.

During the operation, 60 min after the administration of rocuronium, the Anesthesiologist could detect a T1 response. Before the end of the operation, fentanyl (200  $\mu$ g) and flurbiprofen axeti (50 mg) were injected for post-operative analgesia. The propofol and remifentanyl infusions were terminated at the end of surgery. After 10 min, the neuromuscular monitoring remained indicated T1, we administered 2.0 mg/kg (150 mg) sugammadex. Within 180 s of the administration of sugammadex, we detected a T4 response ( $T_4/T_1 = 1.0$ ) and could no longer detect a fade. The patient could lift his head and arms, open his eyes and protrude his tongue. We therefore extubated the patient 300 s after the administration of sugammadex. The post-operative course was uneventful and no respiratory complications were observed.

## DISCUSSION

We have described the first use of sugammadex for the reversal of rocuronium-induced neuromuscular blockade in a patient with KD.

KD is a rare, X-linked recessive, neurodegenerative disorder of the lower motor neurons that is characterized by progressive proximal limb and bulbar muscular.<sup>[3]</sup> The estimated world-wide incidence of KD is approximately one in 40,000 males.<sup>[6]</sup> Patients with KD have a normal life span, but they develop progressive disability with increasing age.<sup>[7]</sup> The clinical manifestations usually begin in the fourth decade of life.<sup>[1,8]</sup> Early symptoms include hand tremor, muscle pain (often associated with increased creatine kinase levels) and premature muscle exhaustion. The loss of lower motor neurons supplying the bulbar musculature results in bulbar symptoms such as difficulty with articulation.<sup>[8]</sup> Up to 47% of patients also experience laryngospasms that occur spontaneously during routine daily activities, but are fortunately self-limited.<sup>[3,4]</sup> Later motor symptoms include proximal extremity weakness (more severe than distal), muscle atrophy and fasciculation (particularly of the lower face), which begin to manifest in the fifth decade of life.<sup>[1,8]</sup> Profound bulbar dysfunction occurs late in the disease process and these patients are at risk for repeated aspiration.<sup>[8]</sup>

Given the weakness from the progressive degeneration of motor neurons in KD, several potential anesthetic risk factors exist, including problems with the acute onset of laryngospasm, hyperkalemia with the use of succinylcholine, increased sensitivity to non-depolarizing muscle relaxants and post-operative respiratory failure or aspiration. Despite this, a Medline search of the available literature from the past 40 years revealed only one case report of the successful use of epidural anesthesia for internal urethrotomy<sup>[9]</sup> and one case series of six patients related to anesthetic management that used a search of medical records from the Mayo Clinic.<sup>[5]</sup> This is the first anesthetic report regarding the general anesthetic management of a patient with KD. This is also the first report of rocuronium and sugammadex being administered to a patient with KD.

Prior to the development of sugammadex, cholinesterase inhibitors were the only option for the reversal of neuromuscular block. Modified I-cyclodextrin sugammadex has been available in Japan since 2010 and its intravascular encapsulating mechanism of action, distant from the neuromuscular junction suggest that it should be ideal for reversing both superficial and deep levels of neuromuscular block.<sup>[10]</sup> The balance of acetylcholine in the neuromuscular nicotinic or muscarinic cleft is not disturbed by the use of sugammadex.

Several previous reports have demonstrated the safety of sugammadex in patients with neuromuscular disease. Four previous case reports have shown that the reversibility of rocuronium-induced neuromuscular blockade with sugammadex was successful in patients with myasthenia gravis.<sup>[11-14]</sup> It has also been reported that sugammadex was effective in the reversal of rocuronium-induced neuromuscular blockade in patients with myotonic dystrophy and transverse myelitis.<sup>[15,16]</sup> Only one case report exists in the literature that describes a pediatric patient with Duchenne muscular dystrophy who experienced the reversal of a rocuronium-induced neuromuscular block with no complications.<sup>[17]</sup>

In our patient, 150 mg sugammadex (2 mg/kg) reversed neuromuscular blockade within 120 s. He had no complications such as hypoxia, hypercapnia, or accelerated muscular weakness after extubation and without recurarization of rocuronium. Sugammadex had rapid and efficient action for the patient with KD that we describe in this case report.

It is unclear whether succinylcholine causes a hyperkalemic response in patients with KD. Patients with severe lower motor neuron disease with the loss of motor function and atrophy are, however, considered to have an increased risk of a hyperkalemic response to succinylcholine.<sup>[18,19]</sup> It appears that the use of succinylcholine should be avoided in patients with motor neuron disease because blood acetylcholine levels may increase the sensitivity to non-depolarizing neuromuscular agents.

In the case management of our patient, we could not use objective neuromuscular monitoring, such as the TOF ratio. We could only use visual and tactile evaluation of the muscle response after TOF stimulation such as counting the number of twitches. There is a significant time gap between the visual loss of fade and the return of the TOF ratio >0.9.<sup>[20]</sup> However, this gap is very short in patients given sugammadex. Therefore, visual evaluation of the muscle response after TOF stimulation is a useful tool with which to evaluate the reversal of neuromuscular block after sugammadex administration.

We were successfully able to use a modified l-cyclodextrin sugammadex on a patient suffering from KD in order to reverse rocuronium-induced neuromuscular blockade. We have come to the conclusion that objective neuromuscular monitoring is an essential factor for those patients.

## REFERENCES

1. Atsuta N, Watanabe H, Ito M, Banno H, Suzuki K, Katsuno M, *et al.* Natural history of spinal and bulbar muscular atrophy (SBMA): A study of 223 Japanese patients. *Brain* 2006;129:1446-55.
2. Kennedy WR, Alter M, Sung JH. Progressive proximal spinal and bulbar muscular atrophy of late onset. A sex-linked recessive trait. *Neurology* 1968;18:671-80.
3. Sobue G, Hashizume Y, Mukai E, Hirayama M, Mitsuma T, Takahashi A. X-linked recessive bulbospinal neuronopathy. A clinicopathological study. *Brain* 1989;112:209-32.
4. Sperfeld AD, Hanemann CO, Ludolph AC, Kassubek J. Laryngospasm: An underdiagnosed symptom of X-linked spinobulbar muscular atrophy. *Neurology* 2005;64:753-4.
5. Niesen AD, Sprung J, Prakash YS, Watson JC, Weingarten TN. Case series: Anesthetic management of patients with spinal and bulbar muscular atrophy (Kennedy's disease). *Can J Anaesth* 2009;56:136-41.
6. La Spada AR, Wilson EM, Lubahn DB, Harding AE, Fischbeck KH. Androgen receptor gene mutations in X-linked spinal and bulbar muscular atrophy. *Nature* 1991;352:77-9.
7. Dejager S, Bry-Gaillard H, Bruckert E, Eymard B, Salachas F, LeGuern E, *et al.* A comprehensive endocrine description of Kennedy's disease revealing androgen insensitivity linked to CAG repeat length. *J Clin Endocrinol Metab* 2002;87:3893-901.
8. Sperfeld AD, Karitzky J, Brummer D, Schreiber H, Häussler J, Ludolph AC, *et al.* X-linked bulbospinal neuronopathy: Kennedy disease. *Arch Neurol* 2002;59:1921-6.
9. Okamoto E, Nitahara K, Yasumoto M, Higa K. Use of epidural anesthesia for surgery in a patient with Kennedy's disease. *Br J Anaesth* 2004;92:432-3.
10. Irie T, Uekama K. Pharmaceutical applications of cyclodextrins. III. Toxicological issues and safety evaluation. *J Pharm Sci* 1997;86:147-62.
11. de Boer HD, van Egmond J, Driessen JJ, Booij LH. Sugammadex in patients with myasthenia gravis. *Anesthesia* 2010;65:653.
12. Unterbuchner C, Fink H, Blobner M. The use of sugammadex in a patient with myasthenia gravis. *Anesthesia* 2010;65:302-5.
13. de Boer HD, van Egmond J, Driessen JJ, Booij LH. A new approach to anesthesia management in myasthenia gravis: Reversal of neuromuscular blockade by sugammadex. *Rev Esp Anesthesiol Reanim* 2010;57:181-4.
14. Petrun AM, Mekis D, Kamenik M. Successful use of rocuronium and sugammadex in a patient with myasthenia. *Eur J Anaesthesiol* 2010;27:917-8.
15. Matsuki Y, Hirose M, Tabata M, Nobukawa Y, Shigemi K. The use of sugammadex in a patient with myotonic dystrophy. *Eur J Anaesthesiol* 2011;28:145-6.
16. Weekes G, Hayes N, Bowen M. Reversal of prolonged rocuronium neuromuscular blockade with sugammadex in an obstetric patient with transverse myelitis. *Int J Obstet Anesth* 2010;19:333-6.
17. de Boer HD, van Esmond J, Booij LH, Driessen JJ. Reversal of rocuronium-induced profound neuromuscular block by sugammadex in Duchenne muscular dystrophy. *Paediatr Anaesth* 2009;19:1226-8.
18. Gronert GA, Lambert EH, Theye RA. The response of denervated skeletal muscle to succinylcholine. *Anesthesiology* 1973;39:13-22.
19. Martyn JA, White DA, Gronert GA, Jaffe RS, Ward JM. Up-and-down regulation of skeletal muscle acetylcholine receptors. Effects on neuromuscular blockers. *Anesthesiology* 1992;76:822-43.
20. Illman HL, Laurila P, Antila H, Meretoja OA, Alahuhta S, Olkkola KT. The duration of residual neuromuscular block after administration of neostigmine or sugammadex at two visible twitches during train-of-four monitoring. *Anesth Analg* 2011;112:63-8.

**How to cite this article:** Takeuchi R, Hoshijima H, Doi K, Nagasaka H. The use of sugammadex in a patient with Kennedy's disease under general anesthesia. *Saudi J Anaesth* 2014;8:418-20.

**Source of Support:** Nil. **Conflict of Interest:** None declared.