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Case Report

Sugammadex-Induced Hypersensitivity Reaction in a Pediatric Patient

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Abstract

We report a case of a 3-year-old boy who administered sugammadex and developed an allergic reaction several minutes after the administration. He developed an increase in airway pressures and a decrease in peripheral oxygen saturation; auscultation revealed widespread wheezing in the lungs. He was successfully treated with immediate administration of methylprednisolone, pheniramine, and theophylline. We assumed an allergic reaction to sugammadex based on the clinical condition of the patient.

Keywords: General anaesthesia, hypersensitivity, sugammadex, child

Introduction

Sugammadex, which has a γ-cyclodextrin structure, is used to reverse steroidal neuromuscular blocking agents. It has the highest affinity for rocuronium and to lesser degree for vecuronium and pancuronium (1).

Sugammadex is used in various countries; however, its approval was questioned because of some allergic and coagulation-related adverse events reported by the US Food and Drug Administration and longer approval process time (2, 3).

Sugammadex is most commonly used in Japan; currently, it is being increasingly used in many European countries. Although it is known as a safe and well-tolerated agent, case reports, particularly from Japan, with anaphylactic or allergic reactions have been increasing lately (4, 5).

Herein we describe a case of hypersensitivity reaction following sugammadex administration to a 3-year-old boy. Written consent has been obtained from his father.

Case Presentation

Otorhinolaryngologists had planned adenoidectomy, bilateral parasynthesis, and bilateral grommet operations for the 3-year-old who weighed 15 kg. He had a history of inguinal hernia repair under general anesthesia with no complications. Preoperative examination revealed no findings.

Following standard monitoring, anesthesia was induced using 50 mg propofol (Propofol 1%, Fresenius, Fresenius Kabi AB, Uppsala, Sweden), 10 mg rocuronium bromide (Esmeron, Hameln Pharmaceuticals GmbH, Germany), and 10 mcg fentanyl (Talinat, VEM İlaç, Tekirdağ). The trachea was intubated using a cuffed tube with 4.0-mm ID. Anesthesia was maintained with sevoflurane and 50% oxygen-air mixture. During the operation, oxygen saturation was maintained at 98%-100%, and $ETCO_2$ was within normal limits. The baseline blood pressure was 91/58 mm Hg and remained in the range of 80-90/40-55 mmHg. The heart rate remained at 100-110 bpm. The total operation duration was 40 min. Despite end-tidal sevoflurane concentration of 0%, the patient was unable to breathe spontaneously. Sugammadex (Bridion, N.V. Organon, Holland) 30 mg (2 mg kg^{-1}) was intravenously administered for residual neuromuscular blockade. After sugammadex ad-

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ministration, an increase in airway pressures and a decrease in peripheral oxygen saturation (SpO_2) were detected; lung auscultation revealed widespread wheezing. Tachycardia of 130-140 bpm developed, and blood pressure was 65/31 mmHg. The SpO_2 values of the patient breathing 100% oxygen kept decreasing; therefore, a possible allergic reaction was suspected, and 20 mg methylprednisolone, 75 mg theophylline, and 15 mg pheniramine were intravenously administered. The lowest observed SpO_2 value was 77%. Approximately 3 min after the drug administration, the SpO_2 values improved and the patient completely recovered; therefore, the trachea was extubated. There were no complications in the recovery room and the ward; thus, the patient was discharged on postoperative day 1.

Discussion

There are some aspects in this case that aroused the suspicion of sugammadex-induced allergic reaction. First, the patient exhibited no reaction to the anesthetic drugs administered 40 min before the operation. Second, he did not have a history of allergic reactions to anesthesia. Finally, respiratory problems were observed immediately after sugammadex administration; therefore, the reaction was confirmed to be sugammadex-induced.

Although a high number of cases of sugammadex-induced hypersensitivity reaction have been reported in adult patients, pediatric cases are rare (6-8). A wide range of doses (1.8-32 $mg \times kg^{-1}$) (9) have been used in the case reports of sugammadex hypersensitivity. Asahi et al. (6) reported that respiratory symptoms and signs were observed 3 min after 40 mg (3.33 $mg \times kg^{-1}$) sugammadex was administered to a 7-year-old boy (height, 100 cm; weight, 12 kg). Takazawa et al. (8) reported a case of 13-year-old male presenting with anaphylactic reaction after 2 $mg \times kg^{-1}$ sugammadex was administered, which is similar to our case.

Tsur and Kalansky (9) reported that sugammadex-induced hypersensitivity reactions were observed in the first 5 min of administration. They detected that the most frequent findings were rash, hypotension, tachycardia, or decreased SpO_2, as found in 80%, 60%, 53%, and 47% of cases, respectively (9). The hypersensitivity reaction in our case was observed in the form of bronchospasm characterized by increased airway pressures, decreased SpO_2, hypotension, and widespread wheezing, which was detected by auscultation just a few minutes after sugammadex administration. Respiratory complications can occur not only by hypersensitivity reactions but also light plane of anesthesia. Additionally, rapid recovery from anesthesia, including neuromuscular blockade, triggers breath-holding, coughing, bucking, oxygen desaturation, and laryngospasm in pediatric patients (10, 11). However, under intubated condition, an increase in airway pressures and a decrease in SpO_2 while ventilated with 100% oxygen suggested an allergic reaction. We did not observe any allergic reactions on the skin.

Adrenaline is the first-line drug for anaphylaxis, whereas steroids, beta-2 adrenergic receptor agonists, and antihistamines are used for further symptomatic treatment (12). We did not use adrenaline because we interpreted that the symptoms were not anaphylactic. Initially, we used steroids, theophylline, and antihistaminic agents to treat bronchospasm. We did not used adrenaline as we observed an improvement in the symptoms.

The clinical diagnosis of anaphylaxis is the recognition of characteristic symptoms and signs with sudden onset after exposure to an allergen. Increased tryptase and histamine levels in blood samples collected within minutes (histamine) to 1-3 hours (tryptase) following clinical onset can be used to support the diagnosis; however, normal tryptase and histamine levels do not rule out the clinical diagnosis. Also even if tryptase levels are within the normal limits, histamine, PAF, PGD2, and LTE4 levels can be elevated in anaphylaxis (12). Skin tests to confirm the clinical diagnosis are recommended; however, their sensitivity and specificity are limited. To ascertain the diagnosis in our case, a skin test was requested; however, the patient's parent refused the necessary permission. The lack of laboratory tests to confirm the hypersensitivity reaction was a weak point; however, the timing of symptoms and their relief following our treatment support the clinical diagnosis of sugammadex-induced hypersensitivity.

Conclusion

Although sugammadex is a safe, effective, lifesaving, and gold standard agent, it is necessary to be careful, particularly in the first 5 min after administration, because it can lead to life-threatening hypersensitivity reactions. In case of a possible hypersensitivity reaction, laboratory and skin tests should be performed to verify the triggering drug.

Informed Consent: Written informed consent was obtained from patients' parents who participated in this case.

Peer-review: Externally peer-reviewed.

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References

1. Keating GM. Sugammadex: A Review of Neuromuscular Blockade Reversal. Drugs 2016; 76: 1041-52. [CrossRef]
2. Schaller SJ, Lewald H. Clinical pharmacology and efficacy of sugammadex in the reversal of neuromuscular blockade. Expert Opin Drug Metab Toxicol 2016; 12: 1097-108. [CrossRef]

3. De Kam PJ, Grobara P, Prohn M, Höppener F, Kluft C, Burggraaf J, et al. Effects of sugammadex on activated partial thromboplastin time and prothrombin time in healthy subjects. Int J Clin Pharmacol Ther 2014; 52: 227-36. [CrossRef]
4. Godai K, Hasegawa-Moriyama M, Kuniyoshi T, Kakoi T, Ikoma K, Isowaki S, et al. Three cases of suspected sugammadex-induced hypersensitivity reactions. Br J Anaesth 2012; 109: 216-8. [CrossRef]
5. Jeyadoss J, Kuruppu P, Nanjappa N, Van Wijk R. Sugammadex hypersensitivity-a case of anaphylaxis. Anaesth Intensive Care 2014; 42: 89-92.
6. Asahi Y, Omichi S, Adachi S, Kagamiuchi H, Kotani J. Hypersensitivity reaction probably induced by sugammadex. Acta Anaesthesiologica Taiwanica 2012; 50: 183-4. [CrossRef]
7. Mimaru K, Gotoh K, Fujiwara K, Nakamura A, Nishimura A, Iijima T. A case report of anaphylaxis associated with sugammadex administration in a pediatric oral surgical case. Journal of Japanese Dental Society of Anesthesiology 2013; 41: 199-200.
8. Takazawa T, Tomita Y, Yoshida N, Tomioka A, Horiuchi T, Nagata C, et al. Three suspected cases of sugammadex-induced anaphylactic shock. BMC Anesthesiol 2014; 14: 92. [CrossRef]
9. Tsur A, Kalansky A. Hypersensitivity associated with sugammadex administration: a systematic review. Anaesthesia 2014; 69: 1251-7. [CrossRef]
10. Shen X, Hu C, Li W. Tracheal extubation of deeply anesthetized pediatric patients: a comparison of sevoflurane and sevoflurane in combination with low-dose remifentanil. Paediatr Anaesth 2012; 22: 1179-84. [CrossRef]
11. Di M, Han Y, Yang Z, Liu H, Ye X, Lai H, et al. Tracheal extubation in deeply anesthetized pediatric patients after tonsillectomy: a comparison of high-concentration sevoflurane alone and low-concentration sevoflurane in combination with dexmedetomidine pre-medication. BMC Anesthesiol 2017; 17: 28. [CrossRef]
12. Simons FE, Ardusso LR, Bilò MB, El-Gamal YM, Ledford DK, Ring J, et al. World Allergy Organization anaphylaxis guidelines: summary. J Allergy Clin Immunol 2011; 127: 587-93. [CrossRef]