

# Sugammadex and anaphylaxis: An analysis of 33 published cases

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## Abstract

In this study, the published sugammadex-induced anaphylaxis reports were reviewed to determine similarities in their presentation during anesthesia. PubMed was searched for sugammadex-induced anaphylaxis without time limitation. Reports were evaluated if they were in English and met the criteria of anaphylaxis determined by the World Allergy Organization. Two independent reviewers extracted and assessed the data using predesigned data collection forms. In total, 23 suitable articles were found and 33 sugammadex-induced anaphylaxis cases were included in the study. The mean age was 43.09 years (from 3–89 years) and 17 (51.5%) of the patients were female. Considering all reported cases, the average onset time of anaphylaxis was 3.08 min, with a median of 3 min (range 1–8 min). The most common signs and symptoms were hypotension, tachycardia, erythema, and desaturation. Of the 20 patients who underwent confirmatory skin testing, 15 had a positive skin reaction for sugammadex. Epinephrine was not given when indicated in about 25% of cases. Sugammadex-induced anaphylaxis onset time was less than 5 min in 92.3% of all the reported cases. Rapid diagnosis and early recognition of signs and symptoms of anaphylaxis are essential for a favorable prognosis. Treatment needs to be started as soon as possible to ensure the best outcome for the patient.

**Keywords:** Adverse event, anaphylaxis, gamma-cyclodextrin, rocuronium bromide, sugammadex

## Introduction

Anaphylaxis is described as a severe, life-threatening, generalized or systemic hypersensitivity reaction. It occurs rarely during surgery and anesthesia but neuromuscular blocking agents, non-steroidal anti-inflammatory drugs (NSAIDs), and antibiotics are considered common causes of anaphylaxis.<sup>[1-3]</sup> The clinical findings are the result of the immediate and continuing release of preformed mediators from mast cells and basophils.<sup>[2,4]</sup> The symptoms and signs such as skin rash, hypotension, tachycardia, and wheezing, present suddenly after the injection of allergic agents.<sup>[1,3,5,6]</sup>

Knowing, as far as possible, the agents that can trigger anaphylaxis is essential for patient safety.

Sugammadex is a synthetic modified gamma-cyclodextrin derivative first designed to selectively bind to the steroidal neuromuscular blocking agent molecule to provide rapid recovery of neuromuscular function.<sup>[7]</sup> Sugammadex is extensively used for reversing the effects of rocuronium and to a lesser extent, vecuronium. It has been in use since 2008 and is now available in many countries. When compared with neostigmine, sugammadex more rapidly reverses rocuronium-induced neuromuscular blocks and has a better safety profile. A recent study reported that patients

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receiving sugammadex had a lower risk of bradycardia, postoperative nausea, and vomiting and showed fewer signs overall of postoperative residual paralysis.<sup>[8]</sup> Despite the many advantages sugammadex provides, one of the major concerns is the allergic reactions that it may trigger.

The first case related to sugammadex-induced anaphylaxis during anesthesia was reported in 2011, and the number of new cases continues to increase each year.<sup>[9]</sup> The aim of the study was to analyze the main characteristics of patients who experienced sugammadex-induced anaphylaxis during anesthesia, the timing of clinical presentation, the treatment preferences, and the outcomes of these patients, as reported in the literature.

## Methods

To investigate this topic, relevant English language studies were identified through PubMed on the 1<sup>st</sup> of May 2019. For our search, we used the following keywords: “sugammadex AND (anaphylaxis OR hypersensitivity)”. No filters were applied.

Using predesigned data collection forms, data were extracted and analyzed independently by two authors from the ultimately included studies. A third author resolved any discrepancies arising during the study selection, data extraction, or trial evaluation. The full texts of the relevant studies were then assessed to determine whether they met the predetermined selection criteria: (1) the full manuscript of the article was written in English and; (2) the study met anaphylaxis criteria according to the World Allergy Organization (WAO). Anaphylaxis was established as adverse effects on two or more body systems.<sup>[10]</sup>

The anaphylaxis cases were analyzed in terms of the following: age, sex, country, year, signs and symptoms, physical examination findings, time from symptom onset to diagnosis, surgical speciality, history of allergies, cardiopulmonary resuscitation (CPR), total amount of sugammadex given, treatment, epinephrine use and route, and results of a skin-prick test or an intradermal test. Patients treated with antihistamines, beta-2 adrenergic agonists, and/or glucocorticoids were considered to have received second-line treatment. If time to reaction or history of atopy or CPR were not documented, these were recorded as “Not reported (NR).” Anaphylactic reaction severity of each case was also graded by the authors based on the four levels of symptom profiles proposed by Mertes *et al.*, namely,<sup>[6]</sup> grade 1 = presence of cutaneous signs; grade 2 = the involvement of at least 2 organ systems, measurable but not life-threatening symptoms; grade 3 = signs

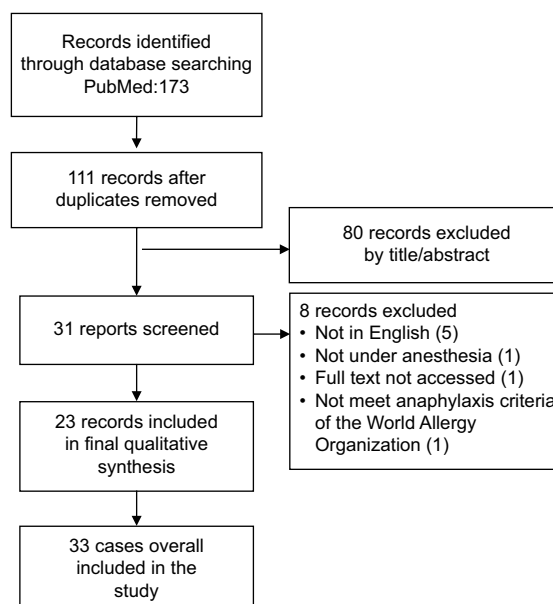
of circulatory and/or respiratory failure/shock; and grade 4 = circulatory or respiratory arrest.

Data were analyzed using the PRISMA methodology.<sup>[11]</sup> A descriptive analysis of the available data estimated the cumulative number of sugammadex-induced anaphylaxis cases and their distribution according to the selected variables. Data were reported as mean (standard deviation), median (interquartile range), range, and number (percentage), as indicated.

## Results

We identified 31 records of previously reported sugammadex-induced anaphylaxis in 45 patients [Figure 1]. Eight records with 12 cases were excluded from the study for the following reasons: (1) the full text of the study was in Japanese in five records; (2) one record did not meet the criteria of anaphylaxis of the WAO; (3) one record was not under anesthesia; and (4) the full text of one record could not be retrieved. The remaining 23 records were analyzed in-depth and their references explored.<sup>[9,12-32]</sup>

A total of 33 cases were reported in the 23 records. The patients involved were mainly women (51.5%) and the average age was 43.09 years (from 3–89 years) [Table 1]. Most cases were adults ( $n = 27$ ). Of the 6 paediatric cases, 4 were teenagers (defined as 11–18 years). The largest contribution of literature was in 2018. Japan reported the majority ( $n = 21$ ), followed by England ( $n = 3$ ). Ten surgical specialties reported cases of sugammadex-induced anaphylaxis, with



**Figure 1:** PRISMA flow diagram. Studies initially evaluated for the current pooled analysis and reasons for exclusion

the most commonly affected specialities being ear-nose-throat surgery ( $n = 7$ , 21.2%), general surgery ( $n = 6$ , 18.2%), and orthopaedic surgery ( $n = 3$ , 9.1%). A history of atopy was reported in only 9 patients (27.3%).

Table 2 details the incidence of signs and symptoms associated with sugammadex anaphylaxis. The most common signs and symptoms were hypotension, tachycardia, erythema, and desaturation. Epinephrine was required in 25 patients (75.7%). Of the 33 patients, only 2 patients (6.1%) received epinephrine by an intramuscular route. In total, 30 (90.9%) patients received second-line treatment for anaphylaxis. Overall, 18.1% ( $n = 6$ ) of the patients required reintubation. Most reactions were categorized as grade III (84.8%) or grade IV (9.1%). One patient (3%) received active chest compressions. Importantly, all patients eventually recovered.

The average time of manifestation of signs and symptoms after sugammadex administration was  $3.08 \pm 1.9$  min, with a median of 3 min (range from 1 to 8 min) for the studies that reported this information ( $n = 25$ ). Postoperative cutaneous testing was performed in 20 (60.6%) patients, and 15 (75%) had skin prick tests and/or intradermal tests that were positive for sugammadex [Table 3]. In addition, 5 patients had positive responses to skin testing with a premixed rocuronium–sugammadex complex. Unfortunately, anaphylaxis developed again during intradermal testing in one patient.

## Discussion

Our analysis revealed that the number of reported sugammadex-induced hypersensitivity reactions is relatively small, with clinical signs that commonly include hypotension, tachycardia, erythema, and desaturation. Most signs appear within the first 5 min of administration.

Epidemiology data for perioperative allergic reactions are variable, with the incidence of serious life-threatening anaphylaxis estimated at 1 in 10000 anesthetic procedures.<sup>[1]</sup> However, because of methodology limitations, the real incidence of anaphylaxis was estimated to be higher. Recently, the occurrence of sugammadex-induced anaphylaxis was calculated to be as high as approximately 1 in 2,500 administrations (0.039%) depending on a retrospective observational study conducted in a single center.<sup>[19]</sup> More than 60% of the cases included in our study were reported from Japan. This large variation depending upon country may be attributed to varying geographical practices, genetics, different approval dates of sugammadex, and variations in reporting rates. Mertes *et al.*<sup>[33]</sup> suggested that the difference in sugammadex-induced

**Table 1: Characteristics of the 33 cases of sugammadex-induced anaphylaxis during anesthesia**

Age, years, mean (SD)	43.12 (22.2)
Female gender (%)	17/33 (51.5%)
Country	
Japan	21 (63.6%)
England	3 (9.1%)
Turkey	2 (6.1%)
Korea	2 (6.1%)
Australia	2 (6.1%)
Spain	1 (3%)
USA	1 (3%)
France	1 (3%)
Time from sugammadex administration to anaphylaxis	
≤ 1 min	8 cases
1-3 min	9 cases
3-5 min	7 cases
More than 5 min	2 cases
Not reported	7 cases

**Table 2: Signs and symptoms of sugammadex-induced anaphylaxis. Values are number (proportion)**

Cardiovascular system	Number of cases (%)	
Hypotension	31	(93.9)
Tachycardia	20	(60.6)
Bradycardia	2	(6.1)
Cutaneous system		
Erythema	17	(51.5)
Rash	9	(27.2)
Edema	7	(21.2)
Respiratory system		
Desaturation	15	(45.4)
Wheezing	8	(24.2)
Increased airway pressure	6	(18.8)
Central nervous system		
Altered mental status	4	(12.1)

anaphylaxis between countries could be due to differences in the total amount of sugammadex used. According to one of the largest sugammadex post-marketing reports, 284 cases of sugammadex-induced anaphylaxis were reported in Japan during the 7-year period after sugammadex was launched.<sup>[34]</sup> A further estimation was that sugammadex had been administered to approximately 10% of the total Japanese population during the 8-year period after its release.

Most reports in the present analysis (92.3%) noted the first sign of a reaction in less than 5 min after sugammadex administration, which was consistent with the rapid development of signs described by other investigators. Hypotension, tachycardia, erythema, and desaturation were found in 93%, 60%, 51%, and 45% of our cases, respectively. Tsur *et al.*<sup>[35]</sup> systematically reviewed the literature of hypersensitivity associated with

**Table 3: Reported sugammadex-induced anaphylactic reactions during general anesthesia**

Reference	Year	Age (y)	Sex	Allergy history	Weight (kg)	SGX Dose (mg)	Time (min)	Laboratory Test for Anaphylaxis	Skin Test for Anaphylaxis
Tomoka <sup>[12]</sup>	2019	18	F	No	57	200	NR	Elevated total Ig E level	Positive SPT for SGX
Allan <sup>[13]</sup>	2019	67	F	Benazepril Ezetimibe Simvastatin Triamterene	115	400	1	Elevated tryptase level	NR
Gunn <sup>[14]</sup>	2019	42	M	Cat hair	78	200	NR	Elevated total Ig E level Elevated tryptase level	Negative IDT for SGX Positive IDT for SGX- ROC complex
Nurdan <sup>[15]</sup>	2018	22	F	Vitamin B	85	340	<1	Normal tryptase level Normal total Ig E level	Not done
Obara <sup>[16]</sup>	2018	73	M	NR	77	200	6	Elevated tryptase level	Positive IDT for SGX Negative IDT for SGX- ROC complex
Alkin <sup>[17]</sup>	2018	3	M	No	15	30	NR	Not done	Not done
Taka <sup>[18]</sup>	2018	65	M	No	NR	100	8	Elevated histamine level Elevated tryptase level Positive LTT for light-exposed SGX in BAT	Not done
Taka <sup>[18]</sup>	2018	29	F	No	NR	100	5	Positive LTT for light-exposed and native SGX in BAT	Not done
Yusuke <sup>[19]</sup>	2018	63	F	Latex	48	100	1	Elevated tryptase level Negative DLST for SGX	Not done
Yusuke <sup>[19]</sup>	2018	60	F	No	54	120	2	Not done	Not done
Yusuke <sup>[19]</sup>	2018	29	F	No	49	200	2	Not done	Not done
Yusuke <sup>[19]</sup>	2018	21	M	No	53	200	1	Not done	Not done
Yusuke <sup>[19]</sup>	2018	46	F	No	89	200	4	Not done	Not done
Yusuke <sup>[19]</sup>	2018	43	F	No	53	200	1	Not done	Not done
Masakazau <sup>[20]</sup>	2017	36	F	No	65	200	NR	Elevated tryptase level	Negative SPT for SGX Negative IDT for SGX Positive SPT for SGX- ROC complex
Eri <sup>[21]</sup>	2016	65	F	No	NR	200	2	NR	Negative SPT for SGX Positive IDT for SGX
Grace <sup>[22]</sup>	2016	50	M	No	95	200	NR	Elevated tryptase level	Negative SPT and IDT for SGX Positive IDT for SGX- ROC complex
Jae <sup>[23]</sup>	2016	35	M	Animal hair	109	200	2	Elevated total Ig E level	Positive SPT for SGX
Nakanishi <sup>[24]</sup>	2016	60	F	No	50	200	3	NR	Positive SPT for SGX Positive SPT for SGX- ROC complex
Kok <sup>[25]</sup>	2016	50	M	NR	NR	200	5	Elevated tryptase level	Positive SPT for SGX Positive IDT for SGX
Kok <sup>[25]</sup>	2016	62	M	NR	NR	400	5	Elevated tryptase level	Positive SPT for SGX Positive IDT for SGX
Kok <sup>[25]</sup>	2016	63	M	NR	NR	100	5	Elevated tryptase level	Positive SPT for SGX Positive IDT for SGX
Tomonori <sup>[26]</sup>	2014	13	M	NR	40	80	NR	Not done	Positive SPT for SGX
Tomonori <sup>[26]</sup>	2014	75	F	NR	71	200	3	Not done	Positive IDT for SGX
Tomonori <sup>[26]</sup>	2014	34	M	NR	62	200	1	Not done	Positive IDT for SGX
Sadlier <sup>[27]</sup>	2014	15	F	Peanut butter	NR	100	NR	Elevated tryptase level	Positive IDT for SGX Negative IDT for SGX- ROC

Contd...

**Table 3:Contd...**

Reference	Year	Age (y)	Sex	Allergy history	Weight (kg)	SGX Dose (mg)	Time (min)	Laboratory Test for Anaphylaxis	Skin Test for Anaphylaxis
Yuko <sup>[28]</sup>	2014	19	F	House dust mite	50		5	Normal typtase level, elevated histamine level	Negative SPT for SGX Positive IDT for SGX- ROC complex
Junko <sup>[29]</sup>	2013	37	M	Shrimp and crab	NR	120	1	Negative DLST for SGX	Not done
Godaj <sup>[30]</sup>	2012	52	F	No	54	100	3	NR	Positive SPT for SGX
Godaj <sup>[30]</sup>	2012	89	F	No	45	100	4	NR	Not done
Yoshinao <sup>[31]</sup>	2012	7	M	No	12	40	3	NR	Not done
Soria <sup>[32]</sup>	2012	62	M	NR	65	150	3	Normal tryptase level	Positive SPT for SGX Positive IDT fo SGX
Menendez <sup>[33]</sup>	2011	17	M	House dust	62	200	1	Elevated tryptase level	Positive SPT for SGX

sugammadex administration in 15 patients and found the most common signs were rash, hypotension, tachycardia, and desaturation. In the operating room, cardiovascular signs of anaphylaxis may be more frequent than skin manifestations due to hemodynamic monitoring of patients.

Epinephrine remains the first-line treatment for perioperative anaphylaxis in all published national anaphylaxis guidelines. The WAO recommends an initial epinephrine treatment by the intramuscular route in the mid-anterolateral thigh as soon as anaphylaxis is diagnosed or strongly suspected, at a dose of 0.01 mg/kg of a 1:1,000 (1 mg/mL) solution, to a maximum of 0.5 mg in adults (0.3 mg in children).<sup>[10]</sup> However, in the presence of shock, the proposed application is a slow intravenous infusion of epinephrine, with dose titration according to the blood pressure and heart rate. In addition, several guidelines are available to help anesthesiologists in treating patients with anaphylaxis during anesthesia. However, some variation is currently present in the recommendations for initial bolus doses of intravenous epinephrine in the existing guidelines on perioperative anaphylaxis. For example, the French guidelines recommend a dose of 10–20 mcg of epinephrine for grade 2 reactions, whereas Scandinavian guidelines recommend initial doses of 10–50 mcg and increased to 100 mcg in cases of severe hypotension.<sup>[5,36]</sup> These differences in recommended intravenous epinephrine doses can lead to confusion in an emergency situation. Fatal outcomes during anaphylaxis are associated with either late or absent administration of epinephrine or with excessive dosing, emphasizing the need for careful titration.<sup>[5]</sup> We found that although all patients developed anaphylaxis of grade 2 and above with an indication of epinephrine administration, epinephrine was not given at all in about 25% of the cases. A greater proportion of patients were treated with a second-line treatment than with epinephrine.

Sugammadex-induced anaphylaxis may present when the patient is already extubated and is being transferred to the

postanesthesia care unit (PACU). In total, 18% of our included cases required emergency reintubation. A neuromuscular blockade after sugammadex administration can be re-established in this type of reintubation situation by one of three options: reuse of rocuronium; use of benzyliisoquinolinium neuromuscular blocking agents (NMBAs), or use of depolarizing NMBAs. Cammu *et al.*<sup>[37]</sup> reported a prolonged re-establishment of the neuromuscular blockade after an increased repeat dose of rocuronium 1.2 mg after a 5 min reversal of sugammadex. However, in the case of sugammadex-induced anaphylaxis, the re-establishment of a neuromuscular blockade with rocuronium may not be a suitable option because, as shown in the present review, some patients also have an allergic reaction to the sugammadex-rocuronium complex. The other option, namely, the use of benzyliisoquinolinium NMBAs such as cisatracurium, is also not appropriate for rapid sequence intubation due to relatively prolonged onset time. In contrast to non-depolarizing NMBAs, a rapid re-establishment of neuromuscular block was reported at 85 s with succinylcholine after the initial use of rocuronium and sugammadex.<sup>[38]</sup>

Our analysis identified a few important findings. Of the 20 patients tested, skin test results were positive in 15 for sugammadex. In addition, 25% of the patients who underwent skin testing had a positive skin reaction to the sugammadex-rocuronium complex. These results indicate that both sugammadex and sugammadex-rocuronium complex may be responsible for hypersensitivity reactions, particularly in a group of patients. Some authors suggested that sugammadex causes anaphylaxis only after it complexes with rocuronium, based on the observation of allergic reactions to a sugammadex-rocuronium complex but not to sugammadex or rocuronium alone.<sup>[39]</sup> These cases support the idea that sugammadex may change its structure and modify drug antigenicity after forming a complex with rocuronium.

This review summarises the previously reported symptom frequencies, outcomes, and timing of sugammadex-induced



anaphylaxis onset after administration. Anesthesiologists should be aware that most of the minor and some of the serious hypersensitivity reactions have likely gone unreported in the literature. Therefore, new studies are warranted to establish the actual incidence of anaphylaxis following sugammadex administration.

Our report has some limitations. Firstly, some studies conducted with pool analysis did not contain all the target parameters. Secondly, our inclusion criteria eliminated studies written in Japanese, even though Japan was the country that reported the most incidences of sugammadex-induced anaphylaxis.

## Conclusion

Anaphylaxis remains a serious and life-threatening adverse event during anesthesia and is probably underdiagnosed. Quick recognition of anaphylactic signs and symptoms is essential for a favourable prognosis. This review showed that approximately 92% of the sugammadex-induced anaphylaxis presented within 5 min, with cardiovascular symptoms, hypotension, and tachycardia being the most common initial presenting manifestations of anaphylaxis during general anesthesia. The number of cases of hypersensitivity to sugammadex is likely to increase with its more widespread use. Thus, anesthesiologists should be familiar with the mechanisms, clinical presentations, and treatment of anaphylaxis.

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## Conflicts of interest

There are no conflicts of interest.

## References

- Harper NJN, Cook TM, Garcez T, Farmer L, Floss K, Marinho S, *et al.* Anaesthesia, surgery, and life-threatening allergic reactions: Epidemiology and clinical features of perioperative anaphylaxis in the 6<sup>th</sup> national audit project (NAP6). *Br J Anaesth* 2018;121:159-71.
- Takazawa T, Mitsuhata H, Mertes PM. Sugammadex and rocuronium-induced anaphylaxis. *J Anesth* 2016;30:290-7.
- Simons FER, Ebisawa M, Sanchez-Borges M, Thong BY, Worm M, Tanno LK, *et al.* 2015 update of the evidence base: World Allergy Organization anaphylaxis guidelines. *World Allergy Organ J* 2015;8:1-16.
- Dewachter P, Faivre C, Emala CW. Anaphylaxis and anesthesia: Controversies and new insights. *Anesthesiology* 2009;111:1141-9.
- Kroigaard M, Garvey LH, Gillberg L, Johansson SGO, Mosbech H, Florvaag E, *et al.* Scandinavian Clinical Practice Guidelines on the diagnosis, management and follow-up of anaphylaxis during anaesthesia. *Acta Anaesthesiol Scand* 2007;51:655-70.
- Mertes PM, Laxenaire MC, Alla F. Anaphylactic and anaphylactoid reactions occurring during anesthesia in France in 1999-2000. *Anesthesiology* 2003;99:536-45.
- Naguib M. Sugammadex: Another milestone in clinical neuromuscular pharmacology. *Anesth Analg* 2007;104:575-81.
- Hristovska AM, Duch P, Allingstrup M, Afshari A. Efficacy and safety of sugammadex versus neostigmine in reversing neuromuscular blockade in adults. *Cochrane Database Syst Rev* 2017;8:CD012763. doi: 10.1002/14651858.CD012763.
- Menéndez-Ozcoidi L, Ortiz-Gómez JR, Olaguibel-Ribero JM, Salvador-Bravo MJ. Allergy to low dose sugammadex. *Anaesthesia* 2011;66:217-9.
- Simons FER, Arduzzo LRF, Bilo MB, Aziz S, Thong BY, *et al.* World Allergy Organization anaphylaxis guidelines: Summary. *J Allergy Clin Immunol* 2011;127:587-93.
- Liberati A, Altman DG, Tetzlaff J, Mulrow C, Gøtzsche PC, Ioannidis JPA, *et al.* The PRISMA statement for reporting systematic reviews and meta-analyses of studies that evaluate health care interventions: Explanation and elaboration. *J Clin Epidemiol* 2009;62:e1-34.
- Matsumura T, Mitani S, Fukayama H. Sugammadex-induced anaphylaxis involving sudden onset of severe abdominal pain. *J Clin Anesth* 2019;57:119-20.
- Escher AR, Cohen JB. Anaphylaxis induced by sugammadex in a patient with papillary serous carcinoma of the uterine adnexa undergoing exploratory laparotomy. *Cureus* 2019;11:1-6.
- Gunn HK, Won SC, Ji EK, Mi JY, Min SK, Mi YK, *et al.* Anaphylactic shock after sugammadex administration, induced by formation of a sugammadex-rocuronium complex. *Korean J Anesthesiol* 2018 [Epub ahead of print]. doi: 10.4097/kja.d.18.00232.
- Bedirli N, Işık B, Bashiri M, Pampal K, Kurtipek Ö. Clinically suspected anaphylaxis induced by sugammadex in a patient with Weaver syndrome undergoing restrictive mammoplasty surgery. *Medicine* 2018;97:1-4.
- Obara S, Kurosawa S, Honda J, Oishi R, Iseki Y, Murakawa M. Cardiac arrest following anaphylaxis induced by sugammadex in a regional hospital. *J Clin Anesth* 2018;44:62-3.
- Çolak A, Yılmaz E, Kiray BK. Sugammadex-induced hypersensitivity reaction in a pediatric patient. *Turk J Anaesthesiol Reanim* 2018;46:66-8.
- Yamada T, Suzuki T, Murase R, Nagata H, Kosugi S. Anaphylactic reactions to native and light-exposed sugammadex suggested by basophil activation test: A report of 2 cases. *A A Pract* 2018;11:181-3.
- Miyazaki Y, Sunaga H, Kida K, Hobo S, Inoue N, Muto M, *et al.* Incidence of anaphylaxis associated with sugammadex. *Anesth Analg* 2018;126:1505-8.
- Yamaoka M, Deguchi M, Ninomiya K, Kurasako T, Matsumoto M. A suspected case of rocuronium-sugammadex complex-induced anaphylactic shock after cesarean section. *J Anesth* 2017;31:148-51.
- Hotta E, Tamagawa-Mineoka R, Masuda K, Taura M, Nakagawa Y, Kanehisa F, *et al.* Anaphylaxis caused by  $\gamma$ -cyclodextrin in sugammadex. *Allergol Int* 2016;65:356-8.
- Ho G, Clarke RC, Sadleir PHM, Platt PR. The first case report of anaphylaxis caused by the inclusion complex of rocuronium and sugammadex. *A Case Rep* 2016;7:190-2.
- Yoo JH, Kim SI, Ok SY, Park SY, Cho A, Han YM, *et al.* Suspected anaphylactic reaction associated with sugammadex - A case report. *Korean J Anesthesiol* 2016;69:413-6.

24. Nakanishi T, Ishida K, Utada K, Yamaguchi M, Matsumoto M. Anaphylaxis to sugammadex diagnosed by skin prick testing using both sugammadex and a sugammadex-rocuronium mixture. *Anaesth Intensive Care* 2016;44:122-4.
25. Ue KL, Kasternow B, Wagner A, Rutkowski R, Rutkowski K. Sugammadex: An emerging trigger of intraoperative anaphylaxis. *Ann Allergy Asthma Immunol* 2016;117:714-6.
26. 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;14:1-5.
27. Sadleir PHM, Russell T, Clarke RC, Maycock E, Platt PR. Intraoperative anaphylaxis to sugammadex and a protocol for intradermal skin testing. *Anaesth Intensive Care* 2014;42:93-6.
28. Yamada Y, Yamamoto T, Tanabe K, Fukuoka N, Takenaka M, Iida H. A case of anaphylaxis apparently induced by sugammadex and rocuronium in successive surgeries. *J Clin Anesth* 2016;32:30-2.
29. Tokuwaka J, Takahashi S, Tanaka M. Anaphylaxis after sugammadex administration. *Can J Anesth* 2013;60:733-4.
30. Godai K, Hasegawa-Moriyama M, Kuniyoshi T, Kakoi T, Ikoma K, Iwasaki S, *et al.* Three cases of suspected sugammadex-induced hypersensitivity reactions. *Br J Anaesth* 2012;109:216-8.
31. Asahi Y, Omichi S, Adachi S, Kagamiuchi H, Kotani J. Hypersensitivity reaction probably induced by sugammadex. *Acta Anaesthesiol Taiwan* 2012;50:183-4.
32. Soria A, Motamed C, Gaouar H, Chemam S, Amsler E, Francès C. Severe reaction following sugammadex injection: Hypersensitivity? *J Investig Allergol Clin Immunol* 2012;22:382.
33. Mertes PM, Ebo DG, Garcez T, Rose M, Sabato V, Takazawa T, *et al.* Comparative epidemiology of suspected perioperative hypersensitivity reactions. *Br J Anaesth* 2019;123:e16-28.
34. Wong JL, Gschwandtner G. Safe gas systems and office-based anesthesia. *The Official Journal of the Anesthesia Patient Safety Foundation. ApsfOrg* 2018;33:17-9. Available from: <https://www.apsf.org/wp-content/uploads/newsletters/2018/june/pdf/APSF201806.pdf>. [Last accessed on 2019 May 13].
35. Tsur A, Kalansky A. Hypersensitivity associated with sugammadex administration: A systematic review. *Anaesthesia* 2014;69:1251-7.
36. Mertes PM, Demoly P. Reducing the risk of anaphylaxis during anaesthesia: Guidelines for clinical practice. *J Investig Allergol Clin Immunol* 2005;15:91-101.
37. Cammu G, De Kam PJ, De Graeve K, Van Den Heuvel M, Suy K, Morias K, *et al.* Repeat dosing of rocuronium 1.2 mg/kg after reversal of neuromuscular block by sugammadex 4.0 mg/kg in anaesthetized healthy volunteers: A modelling-based pilot study. *Br J Anaesth* 2010;105:487-92.
38. Asakura C, Iwasaki H. The use of succinylcholine after sugammadex reversal. *J Anesth* 2016;30:915.
39. Iwasaki H, Renew JR, Kunisawa T, Brull SJ. Preparing for the unexpected: Special considerations and complications after sugammadex administration. *BMC Anesthesiol* 2017;17:1-8.