

## ALLEVIATED ANAPHYLACTIC REACTION TO MUSCLE RELAXANTS DUE TO PREOPERATIVE ADMINISTRATION OF CORTICOSTEROIDS

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Anaphylactic reaction during general anaesthesia represents a rare event in clinical practice with a possible fatal outcome. We present a case of a female patient with no prior history of allergic reactions to rocuronium. Shortly after rocuronium administration, she developed the following signs: tachycardia, low blood pressure and bronchospasm. Skin rash and peripheral signs were absent, probably due to previous premedication. Events like this could be potentially fatal if not recognized and treated in time.

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### Introduction

Anaphylaxis during anaesthesia is a rare event in clinical practice, and it can result in complications and death in 9% of cases. Considering that an anaphylactic reaction during the perioperative period may remain unrecognized, data on its frequency varies from 1:3,500 to 1:445,000 of cases, depending on the country (1, 2). According to research, the most common cause of anaphylaxis during anaesthesia (in as many as 60%–70% of cases) are muscle relaxants, predominantly suxamethonium and rocuronium (1, 3). Cross-reactivity to other muscle relaxants, most often suxamethonium, is present in as many as 65% of patients allergic to

rocuronium (3). Timely recognition of an anaphylactic reaction, its treatment and informing the patient about the event are extremely important.

Allergic reactions to rocuronium are mainly mediated by immunoglobulin E. Given the fact that 75% of allergic reactions to rocuronium occur during the first contact with the agent, there is a suspicion of possible cross-reactivity with apparently unrelated agents as well as with certain foods, cosmetic products and industrial materials (2, 4). Genetic studies show the existence of bypassing of IgE antibodies in situations when a mutation in Mas-related G protein-coupled receptor-X2 is indicated as the cause (5).

Signs of anaphylactic reaction during general anaesthesia do not differ from the symptoms of anaphylaxis in a conscious state, however, considering that a large number of agents are administered in the perioperative period, the signs can be altered and/or masked by hypovolemia, the depth of anaesthesia or the regional blockade (6). Also, there are a large number of other clinical conditions with high incidence during general anaesthesia which can give a similar clinical picture to anaphylaxis.

On this occasion, we present a case report of an anaphylactic reaction most likely caused by rocuronium, which was alleviated by previous premedication and preoperative administration of corticosteroids.

### Case report

A 49-year-old female patient was admitted to the hospital for the procedure of septoplasty,

with a diagnosis of deviated nasal septum. During the preoperative anaesthesiology examination, the patient's general health was assessed, and a clinical examination was performed. The patient was on regular antihypertensive (ramipril, hydrochlorothiazide 2 x 5 mg + 25 mg and bisoprolol 5 mg 1 x 1/2) and endocrinological (levothyroxine-sodium 75 mg) therapy. When it comes to previous surgeries, the patient mentioned having had an appendectomy 10 years ago and a tonsillectomy in childhood. Preoperative laboratory, including thyroid hormones were normal. There were no deviations in the chest X-ray, the electrocardiogram (ECG), and the preoperative clinical examination. The patient denied allergies to food and medical agents, and only mentioned an allergy to "feathers, animal hair and house dust". Anamnesis revealed the reactions exclusively in the form of urticaria. During the patient's previous hospitalization at the Clinic of Otorhinolaryngology, University Clinical Center of Niš, after the induction of anaesthesia and placement of the tracheal tube, there was a sudden drop in oxygen saturation. This event was interpreted by the attending anaesthesiologist as a consequence of the tracheal tube malpositioning while positioning the patient on the operating table. After the repositioning of the tube, saturation stabilization did not occur, and sugammadex was administered. After the clinical parameters stabilized, the patient was awakened and extubated.

After analysing these data from previous intubation and postintubation period, a detailed examination of the patient was undertaken. Spirometry was performed, which showed no deviations, together with an examination by a pulmonologist. The anaesthesiologic examination revealed that the patient was obese with a BMI of 34.72, increased girth and reduced neck height. Neck mobility was preserved, Mallampati score II–III, with normal thyromental distance. The day before the surgery, preoperative bronchodilator therapy (aminophylline NoI/12 h and methylprednisolone 80 mg/12 h) was prescribed to the patient.

Thirty minutes before entering the operating room, premedication was given in the form of an intramuscular injection of 5 mg of midazolam and 0.5 mg of atropine. The response to premedication was satisfactory. Upon entering the operating room, non-invasive monitoring was provided: ECG, pulse oximeter, manometer for blood pressure (BP) measurement. Vital parameters after placing the patient on the operating table were BP 131/82 mmHg, heart rate (HR) 77/min and SpO<sub>2</sub> 97%. After administration of oxygen therapy, saturation improved to SpO<sub>2</sub> 99%. Introduction to general anaesthesia was started with 2 mg of midazolam, 100 mcg of fentanyl and 170 mg of propofol. When loss of consciousness and respiratory suppression were established, manual ventilation with the help of a face mask was started. One minute after the administration

of 50 mg of rocuronium, the HR increased to 125–135/min with occasional ventricular extrasystoles. Blood pressure was measured, and it was as low as 65–75/35–45 mmHg. Clinical examination at that moment showed no visible skin changes or changes in the patient's oxygenation. The patient's peripheral pulse was stable, skin was not flushed nor pale. Two minutes after the administration of the muscle relaxant, the patient was intubated without any difficulties, with a Cormack-Lehane score of 1. Immediately after intubation, resistance during manual ventilation was observed. After placing the patient on the mechanical ventilator, transpulmonary pressure ranged from 25 to 27 mmHg, therefore, manual ventilation was continued. Despite attempts to maintain adequate ventilation, SpO<sub>2</sub> dropped to 88%. Considering dropping in SpO<sub>2</sub> and low BP, 100% oxygen was administered with a flow rate of 6 L/min together with rapid administration of crystalloid fluids. A dose of 50 mcg of phenylephrine was administered on two occasions with close monitoring of BR and HR. This was followed by the rise of BP to 80/40 mmHg, the HR maintained 115–120/min. Saturation rose to 93%. After the systolic BP reached a value above 100 mmHg and HR dropped to 100–105/min, aminophylline NoI was administered in slow bolus.

Surgery was not started until the patient's condition stabilized. After the stabilization of vital parameters, the surgical intervention started, and general anaesthesia was maintained with 1.5–2 Vol% sevoflurane together with a combination of 60% oxygen and 40% air with a flow rate of 3.6 L/min. During the further course of anaesthesia, vital parameters ranged from BP 120–135/65–80 mmHg, HR 85–95/min, SpO<sub>2</sub> 95–97%. The total duration of general anaesthesia was 85 minutes. After the end of the surgical intervention, the surgical sheets were removed when a skin rash was observed in the lower part of the abdomen with extension towards the back. The patient's general condition and vital parameters were stable, without the need for administration of antishock, bronchodilator and antioedematous therapy. The patient was awakened and extubated. After a short postoperative follow-up, the patient was transferred to the ward. Postoperative anamnesis shows that the patient had no subjective complaints except the feeling of "heaviness in the head" the day after surgery. When the patient checked in for the control surgical examination, she was informed about the well-founded suspicion of the allergy to rocuronium with the advice to conduct a more detailed examination in the next period.

## Discussion

Most of the allergic reactions to intravenous anaesthetics develop in the first minutes after the induction of anaesthesia (6). Common symptoms of an anaphylactic reaction are: urticaria,

erythema or oedema, symptoms of the respiratory tract, gastrointestinal tract, cardiovascular system and central nervous system.

The most commonly reported initial symptoms are the absence of peripheral pulse, difficulty in patient ventilation and desaturation with reduced End-Tidal CO<sub>2</sub> (etCO<sub>2</sub>) (7). Clinicians often describe skin changes as the first sign of an intraoperative anaphylactic reaction, however, according to research, the skin reaction to allergen may be absent in the perioperative period, which makes prompt diagnosis difficult (2, 8). The existence of skin signs is very often overlooked due to the covering of visible skin surfaces with surgical sheets (6, 9). Cardiovascular symptoms include hypotension and tachycardia, however, if adequate treatment is not promptly provided, they can soon progress to arrhythmia and cardiovascular collapse (6). The advantage of the occurrence of anaphylactic shock in the operating room is easy and prompt recognition of changes in vital parameters through present monitoring (8, 10).

Bronchospasm occurs less frequently but may be present in patients with asthma or in patients of atopic constitution (6). During the perioperative period, the patient is sedated or under general anaesthesia and is unable to report the presence of signs such as pruritis, hoarseness, dizziness, dysphagia and/or blurred vision (8). The very introduction to anaesthesia leads to the blockade of sympathetic nerves (9), and simultaneously, the administration of medical agents together with previously administered premedication can change the clinical picture of anaphylactic shock and/or lead to diagnosis delay (7). It is important to rule out other clinical conditions that may have similar or the same signs as anaphylaxis. This is extremely important when the patient is under general anaesthesia and when the clinical picture of anaphylaxis is altered or incomplete (7). All this affects the identification and prompt treatment of perioperative anaphylaxis, which contributes to complications and mortality in clinical practice (9).

Meng et al. indicate that they encountered patients with a negative history of the existence of anaphylactic reactions to rocuronium during or after previous surgical interventions (11). This is explained by the fact that the patient was sensitized to the agent during previous general anaesthesia. Our patient previously had two surgical interventions, however, no data were available on the previously used agents. An allergic reaction in the form of bronchoconstriction and a rapid drop in saturation most likely developed during the first hospitalization at the Clinic for otorhinolaryngology. The lack of recognition of an allergy to rocuronium can be explained by the fact that sugammadex was administered as a reversal of the muscle relaxant before more severe signs of anaphylaxis occurred. Several previous case reports have reported stabilization of vital parameters and reversal of

anaphylactic signs after administration of sugammadex. It is believed that sugammadex encapsulates the neuromuscular blocking agent's molecule and thus stops the allergic reaction. However, laboratory and clinical studies did not support this. The conclusion of such discrepancies in science and practice requires additional studies in the near future (8).

When it comes to the second introduction to anaesthesia after the observation of the first sign, e.g., extreme tachycardia, malignant hyperthermia was first suspected. This was immediately ruled out considering the agents used during induction. In the absence of filliform peripheral pulse, skin reactions and cold and moist periphery, hypotension and tachycardia were understood as a complication of hypothyroidism in terms of hypersensitivity to the cardio depressant effects of anaesthetics, although preoperative thyroid hormone values were normal. Cardio-depressive effects in hypothyroidism are due to reduced intravascular volume, reduced preload, reduced baroreceptor response, and reduced cardiac output (12). Also, there is clinical evidence as well as research confirming that prescribing levothyroxine in patients with subclinical hypothyroidism reduces blood pressure values by reducing TSH levels (13, 14).

Symptoms in the form of tachycardia, hypotension and increased resistance in the respiratory tract that occurred in our patient were also reported in other case reports, but they were mostly accompanied by skin changes (5, 15–17). Considering that it is very difficult to recognize an anaphylactic reaction in the absence of skin changes, clinical data indicate that it is necessary to suspect the presence of an anaphylactic reaction if hypotension persists despite the administration of inotropes and vasopressors (10). When it comes to our case, the appearance of skin changes as the first sign was expected given the personal history, and its absence is explained by preoperative preparation and the administration of corticosteroids.

An intraoperative anaphylactic reaction to rocuronium can be life-threatening, and there are a large number of case reports in which cardiopulmonary resuscitation had to be performed (18, 19). Considering the atopic constitution of our patient with a history of developing only mild allergic symptoms, and considering that she had received corticosteroids preoperatively, we believe that the intraoperative anaphylactic reaction we witnessed was mild. There was a relatively quick stabilization of the patient's general condition, and this was maintained until the very end of the intervention. Considering that, the intervention was safely continued.

In the case of suspicion of perioperative anaphylactic reaction, it is necessary to inform the patient and write a report about it. The second step is to refer the patient for histamine/tryptase tests, which are ideally performed within 15

minutes of the reaction onset. In our country, this kind of practice is impossible in smaller medical centers. It is extremely important to verify the occurrence of anaphylaxis, due to the administration of anaesthesia in the future. It is important to point out that cisatracurium has the lowest degree of cross-reaction in patients who have previously experienced an anaphylactic reaction to rocuronium and vecuronium, even if there exists only a reasonable doubt. Therefore, cisatracurium is an alternative muscle relaxant for future surgical interventions (2).

## Conclusion

Perioperative anaphylaxis caused by muscle relaxants is a relatively rare and potentially fatal complication of anaesthesia. For this reason, constant education of anaesthesiologists about possible symptoms and triggers is extremely important. Also, it is necessary to develop official recommendations on further steps if an anaphylactic reaction is recognized intraoperatively. Lack of diagnosis and failure to inform the patient about the existence of suspicion as well as referral for further examination can lead to a fatal outcome after the administration of the agent.

## References

- McDonnell NJ, Pavy TJG, Green LK, Platt PR. Sugammadex in the management of rocuronium-induced anaphylaxis. *Br J Anaesth* 2011; 106 (2): 199–201. [\[CrossRef\]](#) [\[PubMed\]](#)
- Régnier Galvão V, Giavina-Bianchi P, Castells M. Perioperative Anaphylaxis. *Curr Allergy Asthma Rep* 2014; 14(8): 452. [\[CrossRef\]](#) [\[PubMed\]](#)
- Brereton A, Russell WJ. Anaphylaxis to Muscle Relaxants: An Audit of Ten Years of Allergy Testing at the Royal Adelaide Hospital. *Anaesthesia and Intensive Care* 2012; 40(5): 861–6. [\[CrossRef\]](#) [\[PubMed\]](#)
- Li J, Best OG, Rose MA, Green SL, Fulton RB, Capon MJ, Krupowicz BA, Fernando SL. Assessing cross-reactivity to neuromuscular blocking agents by skin and basophil activation tests in patients with neuromuscular blocking agent anaphylaxis. *Br J Anaesth* 2019; 123(1): E144-50. [\[CrossRef\]](#) [\[PubMed\]](#)
- Suzuki Y, Liu S, Kadoya F, Takasaki Y, Yorozuya T, Mogi M. Association between mutated Mas-related G protein-coupled receptor-X2 and rocuronium-induced intraoperative anaphylaxis. *Br J Anaesth* 2020; 125(6): E446-8. [\[CrossRef\]](#) [\[PubMed\]](#)
- Kroigaard M, Garvey LH, Gillberg L, Johansson GO, Mosbech H, Florvaag E, Harboe T, Eriksson LI. Scandinavian Clinical Practice Guidelines on the diagnosis, management and follow-up of anaphylaxis during anaesthesia. *Acta Anaesthesiol Scand* 2007; 51(6): 665-70. [\[CrossRef\]](#) [\[PubMed\]](#)
- Mali S. Anaphylaxis during the perioperative period. *Anesth Essays Res* 2012;6(2):124-33. [\[CrossRef\]](#) [\[PubMed\]](#)
- Takazawa T, Mitsuata H, Mertes PM. Sugammadex and rocuronium-induced anaphylaxis. *J Anesth* 2016; 30(2): 290–7. [\[CrossRef\]](#) [\[PubMed\]](#)
- Zou Y, Shao LJZ, Xue FS. Perioperative anaphylaxis: a potential hazard to the safety of surgical patients. *Chin Med J (Engl)* 2020; 133(5): 609-12. [\[CrossRef\]](#) [\[PubMed\]](#)
- Takazawa T, Yamaura K, Hara T et al. Practical guidelines for the response to perioperative anaphylaxis. *J Anesth* 2021; 35(6): 778–93. [\[CrossRef\]](#) [\[PubMed\]](#)
- Meng J, Rotiroti G, Burdett E., Lukawska JJ. Anaphylaxis during general anaesthesia: experience from a drug allergy centre in the UK. *Acta Anaesthesiol Scand* 2017; 31(3): 281-9. [\[CrossRef\]](#) [\[PubMed\]](#)
- Sudha P, Koshy RC, Pillai VS. Undetected hypothyroidism and unexpected anesthetic complications. *J Anesthesiol Clin Pharmacol* 2012; 28(2): 276-7. [\[CrossRef\]](#) [\[PubMed\]](#)
- He W, Li S, Zhang J, Zhang J, Mu K, Li X. Effect of levothyroxine in blood pressure in patients with subclinical hypothyroidism: A systematic review and meta-analysis. *Front Endocrinol (Lausanne)* 2018; 9:454. [\[CrossRef\]](#) [\[PubMed\]](#)
- Udovicic M, Herrera Pena R, Patham B, Tabatabai L, Kansara A. Hypothyroidism and the Heart. *Methodist Debakey Cardiovasc J* 2017; 13(2): 55–9. [\[CrossRef\]](#) [\[PubMed\]](#)
- Takahashi K, Tanaka S, Watanabe M, Yamakage M. Rocuronium-induced anaphylaxis: a case report. *JA Clin Rep* 2019; 5(1): 81. [\[CrossRef\]](#) [\[PubMed\]](#)
- Hashimoto M, Sato A, Tachi N, Okumura Y, Kadoi K, Harada J, Okuda M. Two Cases of Rocuronium-Induced Anaphylaxis/Anaphylactic Shock Successfully Treated With Sugammadex. *Anesth Prog* 2019; 66(3): 151–5. [\[CrossRef\]](#) [\[PubMed\]](#)
- Kim SM, Oh S, Ryu SA. Treatment of rocuronium-induced anaphylaxis using sugammadex - A case report. *Anesth Pain Med* 2021;16(1):56-9. [\[CrossRef\]](#) [\[PubMed\]](#)
- Takise Y, Kato J, Suhara T et al. Life-threatening rocuronium-induced anaphylactic shock without cutaneous manifestations successfully reversed with sugammadex: a case report. *JA Clin Rep* 2020; 6(1): 95. [\[CrossRef\]](#) [\[PubMed\]](#)
- Macharadze T, Davies A, Fedor I. A Well-Trained Team During Anaphylactic Shock After Rocuronium in a Patient With Aortic Stenosis: A Case Report. *Front Med (Lausanne)*; 6:305. [\[CrossRef\]](#) [\[PubMed\]](#)

Prikaz bolesnika

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## UBLAŽENA ANAFILAKTIČKA REAKCIJA NA MIŠIĆNE RELAKSANTE USLED PREOPERATIVNE PRIPREME KORTIKOSTEROIDIMA

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Anafilaksa tokom anestezije predstavlja redak događaj u kliničkoj praksi, koji može dovesti i do smrtnog ishoda. Prikazan je slučaj bolesnice bez prethodne istorije alergijskih reakcija izazvanih rokuronijumom. Ubrzo nakon primene rokuronijuma, došlo je do pojave tahikardije, niskog krvnog pritiska i bronhospazma. Urtikarija i periferni simptomi su izostali, najverovatnije usled prethodne premedikacije kortikosteroidima. U praksi, situacije poput ove mogu biti fatalne ukoliko se ne prepoznaju i ne tretiraju pravovremeno.

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**Ključne reči:** *anafilaksa, preosetljivost na lekove, hipersenzitivnost, neuromišićni agensi, perioperativni period, rokuronijum-bromid*

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