Case report
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AMELIORATION OF ANAPHYLACTIC REACTION TO MUSCLE RELAXANTS DUE TO PREOPERATIVE ADMINISTRATION OF CORICOSTEROIDS

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ABSTRACT

Anaphylactic reaction during general anesthesia 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 following signs: tachicardia, 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.

Keywords: Anaphylaxis; Drug Hypersensitivity; Hypersensitivity; Neuromuscular Agents; Period, Perioperative; Rocuronium Bromide;

Prikaz bolesnika

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UBLAŽENA ANAFILAKTIČKA REAKCIJA NA MIŠIĆNE RELAKSANTE USLED PREOPERATIVNE PRIPREME KORITKOSTEROIDIMA

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Anafilaksa tokom anestezije predstavlja redak dogadjaj u kliničkoj praksi sa mogućim smrtnim ishodom. Prezentujemo prikaz slučaja pacijentkinje bez prethodne istorije alergijskih reakcija izazvanih Rokuronijumom. Brzo nakon administracije Rokuronijuma pacijentkinja je razvija znake kao što su tahikardija, nizak krvni pritisak i bronhospazam. Urtikarija i periferni simptomi su izostali, najverovatnije usled prethodne premedikacije kortikosteroidima. Dogadjaji u praksi nalik ovom mogu biti fatalni koliko se ne prepoznaju i tretiraju pravovremeno.

Ključne reči: anafilaksa, preosetljivost na lekove, hipersenzitivnost, neuromišićni agensi, perioperativni pregled, reukoronijum-bromid

INTRODUCTION

Anaphylaxis during anesthesia 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 1:3500 to 1:445,000 of cases, depending on the country (1, 2). According to research, the most common cause of anaphylaxis during anesthesia (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 indicate 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 anesthesia 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 anesthesia or the regional blockade (6). Also, there are a large number of other clinical conditions with high incidence during general anesthesia 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 anesthesiology examination, the patient's general health was assessed and a clinical examination was performed. The patient was on regular antihypertensive (Ramipril, hydrochlorothiazide 2x5 mg+25 mg and Bisoprolol 5mg 1x1/2) and endocrinological (Levothyroxine-sodium 75mg) therapy. When it comes to previous surgeries, the patient mentions appendectomy which took place 10 years ago and tonsillectomy which took place 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 that the reactions were exclusively in the form of urticaria. During the patient's previous hospitalization at the Clinic for otorhinolaryngology, University Clinical Center in Nis, after the induction of anesthesia and placement of the tracheal tube, there was a sudden drop in oxygen saturation. This event was interpreted by the attending anesthesiologist 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, patient was awakened and extubated.

After analyzing 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 pneumophthisiologist. The anesthesiological 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 (amp Aminophylline NoI/12h and amp Methylprednisolone 80 mg/12h) was prescribed to the patient.

Thirty minutes before enetring the operating room, premedication was prescribed in the form of an intramuscular injection of amp Midazolam 5 mg and amp Atropine 0.5 mg. 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 SpO2 97%. After administration of oxygen therapy, saturation improved to SpO2 99%. Introduction to general anesthesia was started with amp Midazolam 2 mg, amp Fentanyl 100 mcg and amp Propofol 170 mg. 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 amp Rocuronium 50 mg, 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 not filiform, skin was not flushed nor pale. Two minutes after administration of muscle relaxant, the patient was intubated without any difficulties, with Cormack-Lehane score 1. Immediately after intubation, resistance during manual ventilation was observed. After placing the patient on the mechanical ventilator transpulmonary pressure showed 25-27 mmHg, therefore, manual ventilation was continued. Despite attempts to maintain adequate ventilation, SpO2 dropped to 88%. Considering dropping in SpO2 and low BP, 100% oxygen was administered with a flow rate of 6 L/min together with rapid administration of crystalloid fluids. Phenylephrine 50 mcg 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, amp 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 anesthesia was maintained with Sevoflurane 1.5-2 Vol% together with a combination of 60% oxygen and 40% air with a flow rate of 3.6 L/min. During the further course of anesthesia, vital parameters ranged from BP 120-135/65-80 mmHg, HR 85-95/min, SpO2 95-97%. The total duration of general anesthesia 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 antiedematous 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 carry out a more detailed examination in the next period.

DISCUSSION

Most of the allergic reactions to intravenous anesthetics develop in the first minutes after the induction of anesthesia (6). Common symptoms of an anaphylactic reaction are: urticaria, erythema or edema, symptoms of the respiratory tract, gastrointestinal tract, cardiovascular system and central nervous system.

The most commonly reported initial symptoms are: absence of peripheral pulse, difficulty in patient ventilation and desaturation with reduced End-Tidal CO2 (etCO2) (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 timely diagnosis difficult (2, 8). Very often the existence of skin signs is 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 timely 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 timely 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 anesthesia and is unable to report the presence of signs such as: pruritis, hoarseness, dizziness, dysphagia and/or blurred vision (8). The very introduction to anesthesia leads to blockade of sympathetic nerves (9), and simultaneously 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 anesthesia and when the clinical picture of anaphylaxis is altered or incomplete (7). All this affects

the identification and timely treatment of perioperative anaphylaxis, which contributes to complications and mortality in clinical practice (9).

Meng et al. (11) indicate that they encountered the patients with a negative history of the existence of anaphylactic reactions to rocuronium during or after previous surgical interventions. This is explained by the fact that the patient was actually sensitized to the agent during previous general anesthesia. 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 otorinolaringology. 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 occured. Several previous case reports have reported stabilization of vital parameters and reversal of anaphylactic signs after administration of Sugamadex. It is believed that Sugammadex encapsulates the neuromuscular blocking agents 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 second introduction to anesthesia, 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 filirophm 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 cardiodepressant effects of anesthetics, despite the fact that preoperative thyroid hormone values were normal. Cardiodepressive 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 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 the 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 to 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 anesthesia 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 anesthesia. For this reason, constant education of anesthesiologists 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.

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