

Diagnosis and Management of Rocuronium-induced Perioperative Anaphylaxis

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Abstract: Introduction - Perioperative anaphylaxis is a hypersensitivity reaction that occurs after exposure to drugs used for anaesthesia during a surgical procedure. The most common triggers are neuromuscular blocking agents and antibiotics. Case report - A 71-old man, with a history of anaphylaxis during previous anaesthesia, was scheduled for elective coronary surgery. The clinical signs included skin rash, swelling of the upper part of the body with angioedema of the eyelids and lips, without bronchospasm. Based on the assumption that rocuronium was the most likely causative agent, percutaneous coronary intervention was performed during the same hospitalization. After recovery, he was sent for a prick skin test and intradermal test, where sensitivity to rocuronium and insensitivity to the anaesthetics used were determined. Two months later, he developed an acute myocardial infarction. Chronic total occlusive percutaneous coronary intervention was attempted, but without optimal results, so the patient was prepared for elective surgery. Due to potential further complications during anaesthesia, the medical team decided to send him for a skin allergy test for neuromuscular blocking agents. The only neuromuscular relaxant available was Cisatracurium, and it was tested for sensitivity by intradermal test. The intradermal test showed insensitivity to Cisatracurium and Suxamethonium chloride. Conclusion - Early recognition and management of anaphylaxis is based on clinical presentation. The diagnosis by in-vivo and in-vitro tests is useful to determine the cause of anaphylactic reaction and safe alternatives for future anaesthesia.

Keywords: Rocuronium, Anaphylaxis, Perioperative Period, Drug Hypersensitivity, Anesthesia, Signs and Symptoms, Skin Tests, Cisatracurium

1. Introduction

Anaphylaxis is a severe, systemic hypersensitivity reaction that occurs suddenly after exposure to a provoking agent and may cause death [1]. Perioperative anaphylaxis is the result of drugs or substances used for anesthesia and surgery. Neuromuscular blocking agents and antibiotics are the most common triggers. Early recognition and management of the anaphylaxis are crucial. Still, anaphylaxis is usually unrecognized and managed improperly. Diagnosis and management are difficult because reactions occur promptly and suddenly. Skin tests with in-vitro tests remain the measure for detection of suspected agent, pathophysiological mechanism, safe alternatives, and include contact of the mast cells of patients who experience anaphylaxis to the suspected immune trigger. The aim of this case report was to describe

clinical presentation and management of perioperative anaphylaxis as well as approach for the accurate diagnosis of the causative drug.

2. Case Report

A 71-old – male (weight 70 kg and body mass index 22, 36), American Society of Anesthesiologist physical status Class IV, was scheduled for elective coronary artery bypass graft surgery. He had a history allergic reaction during anaesthesia 11 months before in our hospital when he was scheduled for the same surgery. The patient's anaesthesia record from the previous surgery showed that he received 5 mg Bisoprolol and 0, 25 mg/kg Midazolam preoperatively. General anaesthesia was induced with 80 mg Lidocaine, 50 mcg Sufentanil, 2 mg Midazolam, 60 mg Propofol and 70 mg

Rocuronium. After the medications were given, he developed skin rash and edema on his head, neck and chest. With possible diagnosis of anaphylaxis, Methylprednisolone 1 mg/kg was given intravenously. Bronchospasm after tracheal intubation was not recorded and he remained haemodynamically stable. After tracheal intubation, angioedema of eyelids and mouth occurred, and another dose of Methylprednisolone 1 mg/kg was given together with Chloropyramine 40 mg intravenously with continuous infusion of diluted Adrenaline 0.1 mcg/kg/min. He responded to the treatment and the swelling of the face and body decreased gradually. The surgery was suspended and he remained orotracheally intubated and transferred to the Intensive Care Unit where he remained haemodynamically stable. He did not require any inotropes and after 3 hours he was extubated with satisfactory blood gas analyses. He was transferred to the ward the next morning. After 4 days, percutaneous coronary intervention was performed successfully and stents were placed in the ramus circumflexus artery and ramus intermedius artery.

He was sent for prick skin test and intradermal test after 10 weeks to an Allergy and Immunology Clinic. It was found that he was not sensitive to Lidocaine, Bupivacaine, Atropine, Neostigmine, Fentanyl, Midazolam, Propofol, Midarine, Meropenem, and Metronidazole. The patient was a diabetic on combined therapy with Insulin and oral hypoglycemic drugs, but was also taking oral medications for hypertension (Bisoprolol, Ramipril, Trimetazidine, Furosemide, Spironolactone) and hyperlipoproteinemia (Rosuvastatine). The medical history revealed that the patient underwent tonsillectomy and inguinal hernia repair on right side, 30 and 20 years ago, respectively. However, there were no records on the type of anaesthesia he had received. There was no history of any drug allergy, but he reported edema of the face after consuming products that contain propolis and edema of mouth after a bee sting. One month after the skin test was performed the patient developed acute myocardial infarction of the anterior wall and was hospitalized. During that hospitalization, coronary angiography procedure showed triple vessel coronary artery disease. Optimized results with chronic total occlusion percutaneous coronary intervention could not be achieved, so coronary bypass surgery was recommended. Because of persisting symptoms after myocardial infarction (chest pain, fatigue, dizziness, syncope) the patient was prepared for surgery. He was sent to Allergy and Immunology Clinic where examination on neuromuscular blocking agents was performed and confirmed immune reaction to Rocuronium (generalized urticaria). It was strongly recommended to avoid the triggering agent and other aminosteroid neuromuscular blocking agents (Pancuronium). There were no clinical signs of early or late allergic reaction to Suxamethonium chloride and Cisatracurium, so they could be used. The patient was hospitalized for a planned surgery. The only alternate neuromuscular blocking agent available to us was Cisatracurium. According to allergologist's recommendation, he was received Methylprednisolone 40 mg, a Levocetirizine

and a Famotidine tablet the day before surgery. All precautionary measures were taken, drugs such as adrenaline, steroids and antihistamines were loaded in syringes and equipment required for resuscitation was kept ready. The premedication included intravenous Methylprednisolone 40 mg, 1 intramuscular Chloropyramine vial, and 1 intravenous Pantoprazole vial and the patient was transferred to the operating room. The electrocardiogram, blood pressure, pulse, spO₂ and capnography were monitored and intravenous access was established. His preoperative blood pressure was 150/74, pulse 88/min and SpO₂ was 98% on room air. The patient was preoxygenated with 100% oxygen. General anesthesia was performed with 100 mcg Fentanyl, 2 mg Midazolam, and 60 mg Propofol. Muscle relaxation was achieved by infusion of Cisatracurium (0.2 mg/kg). After 3 minutes of ventilation, the patient was intubated and the position of orotracheal tube was checked. Anesthesia was maintained by sevoflurane 0.8-1.5% in 1:2 mixture of oxygen and air. Muscle relaxation was maintained with 6 supplemental bolus doses of Cisatracurium (0.03 mg/kg). Intraoperatively, patient remained haemodynamically stable. After Protamine administration, 100 mg Hydrocortisone was administered intravenously to slow down the patient's immune system and prevent allergic reaction. The surgery lasted 180 minutes and total anesthesia 205 minutes. The patient was moved in Intensive Care Unit where he maintained haemodynamically stable. After 3 hours he was extubated with satisfactory blood gas analyses. The patient was moved to the ward and discharged from hospital 7 days later. He received written information about all procedures and tests that were performed, safe and unsafe drugs and anaesthesia procedures.

3. Discussion

Perioperative anaphylaxis is defined as a life-threatening hypersensitivity reaction which may be a result of non-allergic or allergic reaction [2]. The incidence of perioperative anaphylaxis varies from one in 18600 to one in 353 with geographical variability [3].

Neuromuscular blocking agents and antibiotics are the most common triggers and usually occur after induction of anaesthesia. Rocuronium is the most common cause of perioperative anaphylaxis compared to other neuromuscular blocking agents [3, 4]. The other triggering agents that may cause perioperative anaphylaxis are hypnotics, opioids, local anesthetics, latex, nonsteroidal anti-inflammatory drugs, disinfectants, dyes, colloids, blood products, aprotinin, and protamine sulphate [3, 5]. The diagnosis of perioperative anaphylaxis is usually made by clinical signs, their manifestation, and the time appearance after drug administration. Clinical presentation can range from mild symptoms to serious illness and mortality. Skin manifestations of perioperative anaphylaxis are often present.

Unexpected perioperative hypotension, bradycardia, asystole and bronchospasm can also occur [6].

Ring and Messmer classification is used to describe

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