Amikacin-triggered anaphylaxis: Should we go for skin test?

Sir,

Antibiotic triggered anaphylaxis has been regularly reported in the perioperative period. Penicillins, cephalosporins and other β-lactam antibiotics, vancomycin, bacitracin, andclindamycin are in the list.[1] Amikacin is the commonly used antibiotic before any urogenital instrumental procedure to prevent gram-negative endotoxemia. An earlier report showed that it induced eosinophilia and mild systemic symptoms syndrome.[2] Anaphylaxis to amikacin is very rare and has never been reported in the literature. After obtaining consent from the patient, we decided to report the case.

A 59-year-old healthy male (weight 72 kg) with normal airway and spinal anatomy, a case of carcinoma bladder, was posted for transurethral resection of bladder tumor. His renal function was within normal limits. He had a history of taking cefoperazone 6 months ago for the treatment of complicated urinary tract infection. He never received amikacin before. After attaching the basic monitors, subarachnoid block (SAB) with 2.5 ml of bupivacaine heavy 0.5% with 25 mcg fentanyl was given at the level of L3–L4. Highest spinal level achieved was up to T8. Hemodynamics was well maintained with heart rate of 60-80/min. Intravenous (IV) injection of amikacin 1 g was given before instrumental manipulation of the urinary tract, 18 min after SAB. Within 2 min of amikacin injection, he complained of pruritus in hands and nausea. He developed rashes in his upper limb, chest, and abdomen [Figure 1], followed by breathlessness, tachycardia, severe hypotension, and cardiovascular collapse. On auscultation, bronchospasm and pulmonary edema were suspected. Immediately, hydrocortisone, promethazine, and ranitidine were administered in bolus form, which was followed by initiation of salbutamol nebulization. Adrenaline (ADR) 0.5 mg bolus, followed by 0.1-0.5 mcg/kg/min infusion was started and titrated. Fluid resuscitation was done with minimum volume of normal saline. He was intubated and oxygenated with 100% oxygen. End-tidal carbon dioxide curve showed obstructive pattern with high peak airway pressure. Glidescopic view showed no laryngeal edema. He was shifted to the ICU and invasive monitoring was secured. With ADR high-dose infusion (2 mcg/kg/min), his blood pressure was not maintained. Hemodynamics became stable after starting vasopressin infusion. The levels of serum mast cell tryptase, histamine, and immunoglobulin E (IgE) were high. He was managed conservatively. Inotropic and vasopressor support was reduced and he was extubated safely. On subsequent days, no complications occurred, and he was discharged from the hospital within 14 days with attached in allergy and immunology clinic.

Antibiotic-related anaphylaxis usually occurs within minutes after IV injections. In our case, amikacin was injected 18 min after subarachnoid bupivacaine injection. Bupivacaine has never been reported as an agent causing anaphylaxis, so amikacin is likely to be the causative agent in this scenario. Perioperative anaphylaxis was previously reported with antibiotics, contrast media muscle relaxants, latex, colloids, IV inducing agents, opioids, aprotinin, ester local anesthetics, protamine.[1] Anaphylaxis to erythromycin by cross-sensitivity was also reported.[3] It was type 1 hypersensitivity reaction with clinical classification class IV.[4] After the first exposure of antigens in the body, the IgE secreted from B lymphocytes [class switching by interleukin-4 (IL-4)] is attached with the cell surface of mast cells of the tissue and basophiles in blood. After the second exposure of the same antigens, there is cross-linking between the IgEs of a number of mast cells through bridging antigens, causing cascade of release of inflammatory mediators.[5] Eight to ten percent risk of cross-sensitivity has been reported between penicillins and cephalosporins due to lactam ring.[6] Cross-reactivity between aminoglycoside (AGS) and cephalosporin has never been reported. Here the patient received the preparation of amikacin containing preservatives methylparaben (0.08% v/v) and propylparaben (0.02% v/v

Figure 1: Skin rash after amikacin exposure

and is named Lupamik (Lupin Ltd, Mumbai, India). It is thought that para-aminobenzoic acid or methylparaben may be the causative agent triggering anaphylaxis. In our case, it may be due to the cross-reactivity between antibiotics or may be due to the structural similarity of AGS with the agents used daily like tooth paste, soap, cosmetics, food, or any other drugs.[7] To prevent antibiotic-related anaphylaxis, considering previous history is very important. Skin test is commonly performed before prescribing β-lactam antibiotics in the perioperative period. But skin test has never been performed before amikacin injection. From a safety point of view, skin sensitivity test may be performed before any AGS injection. So, our question is: Should we proceed for skin test before amikacin/AGS injection? Literature will reply in future and large-scale studies will answer our quest.

Sukhen Samanta, Sujay Samanta[1], Abhishek Jha[1]

Department of Critical Care Medicine, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, Uttar Pradesh, [1]Department of Anaesthesia and Intensive Care, Post Graduate Institute of Medical Education and Research, Chandigarh, India

Address for correspondence:
Sukhen Samanta, Department of Critical Care Medicine,
Sanjay Gandhi Post Graduate Institute of Medical Sciences,
Lucknow - 226 014, Uttar Pradesh, India.
E-mail: dr.sukhensamanta@gmail.com

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