

Anaphylactic Shock Following Cataract Surgery: A Documented Intracameral Cefuroxime Allergy

Mahiat C¹, Robaye S², Levecq L³, Dumesnil D³, Sohy C¹

¹*Pulmonology Department, CHU UCL Namur, Université catholique de Louvain, Yvoir, Belgium*

²*Anesthesiology Department, CHU UCL Namur, Université catholique de Louvain, Yvoir, Belgium*

³*Ophthalmology department, CHU UCL Namur, Université catholique de Louvain, Yvoir, Belgium*

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Intracameral cefuroxime is recommended at the end of cataract surgery, since it has been shown to substantially reduce the rate of postoperative endophthalmitis, a severe postoperative infectious complication [1]. Intracameral cefuroxime is well tolerated, with few adverse events reported [1]. The development of topical anesthesia means that more and more cataract surgeries are performed in outpatient centers [2], with fewer and fewer ophthalmologists considering the presence of an anesthetist to be necessary [3]. We report a case of documented life-threatening immediate hypersensitivity reaction to cefuroxime after cataract surgery.

An 81-year-old woman with no history of food or drug allergy underwent phacoemulsification and intraocular lens implantation in both eyes under topical anesthesia (3-week interval between procedures). The substances administered during the interventions were as follows: Minims oxybuprocaine hydrochloride 0.4% eye drops; Iso-betadine (polyvidone iodine) 5% eye irrigation solution; intracameral Mydrane (tropicamide 0.04 mg/0.2 mL; phenylephrine chlorhydrate 0.62 mg/0.2 mL; lidocaine chlorhydrate 2 mg/0.2 mL); Healon EndoCoat, a viscoelastic device containing sodium hyaluronate; intracameral Apropokam (cefuroxime 1 mg/0.1 mL); and Maxitrol eye drops and ointment (dexamethasone 1 mg/mL; neomycin sulfate 3500 IU/mL; polymyxin B sulfate 6000 IU/mL). The intervention on the right eye was completed without complications. Three weeks later, the same procedure was repeated on the left eye. At the end of the intervention, the patient lost consciousness. Her blood pressure and heart rate were 40/20 mmHg and 140 bpm, respectively. Immediate management by the anesthetist comprised intravascular filling, intravenous epinephrine, and orotracheal intubation. The patient was then admitted to the intensive care unit. Within a few minutes she had developed erythematous macules on the limbs and swelling of the lips and eyelids. Refractory hypotension was treated with intravenous norepinephrine and epinephrine for 21 hours. Serum tryptase

was elevated at 31.1 µg/L (normal value, <14 µg/L) at that time. Basal serum tryptase measured 16 weeks later was normal (6.6 µg/L). Anaphylactic shock due to a substance received during the cataract surgery was suspected. Two days later, the patient had fully recovered and was discharged with a well-tolerated 7-day course of amoxicillin/clavulanic acid for suspected respiratory infection. No ocular sequelae have been reported to date.

Four months later, after obtaining the patient's informed consent, we performed diagnostic skin prick tests (SPTs) on the forearm, as previously described [4] and with some modifications, in a day hospital near the intensive care unit and under close medical supervision. We tested the medications used during surgery, namely, cefuroxime (5 mg/mL in 0.9% saline), a panel of cephalosporin derivatives (ie, cefazolin, ceftriaxone, cefepime) at 100 mg/mL in saline (concentration already used in more than 50 patients in our center without skin irritation), and latex (ALK-Abello BV). All the compounds were tested at the same time. Ten minutes after the SPTs, the patient developed malaise, dyspnea, palmar pruritus, labial edema, and erythema of the right arm. Blood pressure fell to 80/40 mmHg (150/80 mmHg before the tests). Intravascular filling, intravenous epinephrine, corticosteroids, and oral antihistamine were administered immediately, and the patient's condition improved quickly. SPT results were positive for cefuroxime (15×15 mm wheal reaction), ceftriaxone (9×8 mm), and cefepime (10×11 mm) and negative for all other drugs. Histamine (ALK-Abello BV, 10 mg/mL, 6×5 mm) was used as a positive control and saline solution as a negative control. In vitro assays for specific IgE antibodies to penicilloyl G, penicilloyl V, amoxicilloyl, ampicilloyl, cefaclor, and latex (ImmunoCAP Specific IgE, Thermo Fisher Scientific) were performed according to the manufacturer's instructions. The results were all negative (≤0.1 kU_A/L).

The patient experienced 2 severe anaphylactic reactions: one after cataract surgery and another (less severe) after SPTs. SPTs provided convincing evidence that cefuroxime was the causal agent of the anaphylactic shock following surgery. SPTs also identified cross-sensitization to other cephalosporins with the same R1 side chain [5]. As the antibiotics were tested at the same time, cross-reactive cephalosporins may have also contributed to the systemic reaction following SPTs.

This report demonstrates that anaphylactic reactions can be induced by drugs injected into the anterior chamber of the eye. Interestingly, the first intracameral cefuroxime injection did not trigger allergic manifestations. Since the patient had never received cefuroxime before, we hypothesize that sensitization occurred during the first procedure. Under normal conditions, the blood–aqueous barrier restricts entry of inflammatory and immune cells into the eye and separates the anterior chamber from the bloodstream [6]. However, as this barrier is ruptured during cataract surgery [6], immune cells could be exposed to cefuroxime, leading to sensitization in the first procedure and anaphylactic reaction in the second.

Our findings should make clinicians aware that perioperative anaphylactic reactions may not always be predictable and can occur during surgery under topical anesthesia. The presence of an anesthetist is useful for management of such life-threatening complications.

Table. Cases of Anaphylactic Reactions Following Administration of Intracameral Cefuroxime

Author, year	Age, y	Previous known allergy	First/ second surgery	Manifestations	Endpoint	Anesthetist present in operating room	Allergic confirmation
Villada et al 2005 [7]	68	Ampicillin	Second (first: no antibiotic used)	Hypotension, dyspnea, eyelid swelling	Recovery	Yes	Not available
Moisseiev et al 2013 [8]	64	Penicillin	Not specified	Hypotension, dyspnea, skin rash, tongue swelling, vomiting, lethargy	Recovery	No	Not available
Kędziora et al 2016 [9]	Not reported	Cefuroxime	Not specified	Hypotension, dyspnea, respiratory arrest, skin rash, agitation, loss of consciousness	Recovery	Yes	Yes (tests not specified)
Present case	81	None	Second	Hypotension, skin rash, lips and eyelids swelling, loss of consciousness	Recovery	Yes	Yes (skin prick tests)

To our knowledge, 3 cases of anaphylactic reactions to intracameral administration of cefuroxime during cataract surgery have been reported to date [7-9] (Table). The results of allergy testing were not available in 2 of the cases. The role of cefuroxime allergy was based only on a history of penicillin allergy [7,8], although there is usually no cross-reactivity between penicillin and cefuroxime because of different R1 side chains [5]. Moreover, other drugs administered during cataract surgery might also have triggered the systemic reactions. In the third case, the patient had a history of anaphylactic reaction after intravenous and oral administration of cefuroxime [9]. The patient was referred to an allergist, who confirmed β -lactam allergy, although the details of the allergy tests were not reported [9]. Our report emphasizes the need to accurately identify the causal agent involved in the development of anaphylactic reactions after cataract surgery and to explore potential cross-sensitization by performing appropriate allergy tests in order to propose accurate avoidance measures. These tests should be performed under close medical supervision, given the risk of severe anaphylactic reactions, as reported here and elsewhere [10]. If systemic reactions occur after administration of a small quantity of antibiotics to the eye, SPTs should be performed more cautiously at higher dilutions.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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Carine Sohy

Pulmonology department
CHU UCL Namur, Université catholique de Louvain
Avenue Docteur Therasse 1
5530 Yvoir, Belgium
E-mail: carine.sohy@chuuclnamur.uclouvain.be