Tolerability of intracameral cefuroxime during cataract surgery in case of penicillin allergy

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Summary
Introduction. – Since the results of the ESCRs study in 2007 and then the AFSSAPS recommendations of 2011, postoperative endophthalmitis prophylaxis in cataract surgery has evolved toward intracameral cefuroxime. Penicillin allergy is frequent and is not considered as a contraindication to cefuroxime injection, but cross-reactions do exist. The goal of this study was to assess the tolerability of intracameral cefuroxime in patients with a penicillin allergy. Materials and methods. – In this monocentric open prospective study, adult patients undergoing cataract surgery and declaring themselves penicillin-allergic were included. A subcutaneous test of cefuroxime was performed preoperatively. If negative, patients received the intracameral injection of cefuroxime at the conclusion of the surgical procedure. The primary assessment criteria, evaluated on the day after the surgery, was the occurrence of allergic reactions. Results. – Forty-eight eyes of 40 patients, 72 ± 8 years old, were included. Forty-three skin tests were performed: 1 was positive and one was unreliable. Thirty-six patients were examined in our center the day after the surgery: 2 presented a conjunctival allergic reaction. No severe anaphylactic reaction was reported.

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Introduction

The study performed by the European Society of Cataract and Refractive Surgeons (ESCRS) in 2007 [1] proved the efficacy of an intracameral injection of cefuroxime to prevent postoperative endophthalmitis after cataract surgery. In France, this intracameral injection has been validated in 2011 by the recommendations of the French Agency for Safety of Health Products for antibioprophylaxis in intracocular surgery [2].

Penicillin allergy is frequent in the general population, concerning about 10% of the patients. Cefuroxime is a second-generation cephalosporin. Because penicillin and cephalosporin molecules share some common characteristics, such as identical side chains, an allergic cross reactivity is possible (Fig. 1). That is why a cephalosporin administration in a penicillin allergic patient had to be considered with caution.

In clinical practice, it seems that a penicillin allergic patients can safely receive an intracameral injection of cefuroxime during cataract surgery. In a French series of 2289 patients [3], as well as in the ESCR5 study [1], no allergic reaction was reported. So, the most recent guidelines recommend the use of cefuroxime in penicillin allergic patients [4]: only cephalosporin allergy is considered as a contraindication. However, two cases of anaphylactic reaction have been reported in patients with penicillin allergy but no previous cephalosporin allergy [5,6]. Rupture of blood aqueous barrier during the procedure may lead to an allergic reaction in sensitive patients [6]. Surgeons as well as
anesthesiologists seem to prefer to withhold this injection most of the time [7]. Nevertheless, it could certainly represent a loss of chance regarding endophthalmitis prevention. As an option for more safety, Moiseiev et al. [5] proposed a preoperative screening for cefuroxime hypersensitivity using a prick-test.

The aim of this study was to assess the tolerance of the intracameral injection of cefuroxime during cataract surgery in patients with a penicillin allergy and a negative cefuroxime preoperative screening.

Methods

In this prospective study, all adult patients undergoing cataract surgery (either cataract surgery or combined cataract and trabeculectomy surgery) and declaring having a penicillin allergy during preoperative appointment with the surgeon and/or the anesthesiologist. The clinical manifestations of this allergy were not reported. The inclusion time frame was 18 months. Patients were not included if they reported a cephalosporin allergy. Information and agreement of patients were recorded during the anesthesiologist preoperative consultation and repeated immediately before surgery. In case of peroperative complication, such as rupture of the posterior capsule, or in case of rejection by the surgeon or the anesthesiologist present in the operating theatre, the patient was excluded from the study.

A preoperative test was performed just before the surgery by the anesthesiologist with a subcutaneous injection of 0.1 mL of cefuroxime in the shoulder. The cefuroxime was prepared by the hospital's pharmacy as ready-to-use syringes. Erythema and cutaneous induration at the site of injection was measured in order to be interpreted by the anesthesiologist as positive or negative. Then the anesthesiologist proceeded to the locoregional anesthesia of the eye with a peribulbar injection of lidocaine.

If the test was negative and if there was no operative complication, the patient received an intracameral injection of 0.1 mL of cefuroxime at the end of the procedure. The cefuroxime was also prepared by the hospital's pharmacy as ready-to-use syringes. In case of a positive preoperative test, no cefuroxime was injected. In accordance with antibioprophyaxis recommendations, those patients received an oral fluoroquinolone only if there was any risk factor of infection, such as diabetes.

The primary assessment criteria was evaluated the day after surgery and was the presence of an allergic reaction. Immediate reactions in the operating room and reactions assessed the day of evaluation were reported, including general (anaphylaxis, bronchospasm), cutaneous (itching, erythema), conjunctival (palpebral edema, chemosis, conjunctival hyperemia, ocular itching) and intraocular (anterior chamber or vitreous inflammation) reactions. Every noted inflammatory disorder was considered as an allergic manifestation.

The secondary assessment criteria were the type and severity of observed reaction and the number of positive cefuroxime preoperative tests.

Results

Forty-eight eyes of 40 patients, 72±8 years old, were included in the study: 11 men and 29 women. Forty-five patients underwent a cataract surgery by phacoemulsification while 3 patients had a combined surgery of cataract and trabeculectomy, 25 on the right eye and 23 on the left eye. Nine surgeons and 1 anesthesiologist contributed to the study.

Forty-three cefuroxime subcutaneous tests were performed: 1 was unreliable and 1 was interpreted as positive. Those 2 patients had no cefuroxime intracameral injection. Another 6 patients did not receive the injection: 4 because of a posterior capsular rupture, 1 because of rejection by the surgeon, and the remaining one was not itemized. Thus, 40 of the 48 eyes received the intracameral cefuroxime at the end of the procedure.

Among the 40 injected eyes, 36 were examined in our centre the day after surgery. Two patients (5%) reported a conjunctival reaction. The first one presented a conjunctivitis with conjunctival hyperemia, ocular itching and papillary reaction. The second one had only a chemosis. Neither anaphylactic reaction nor severe inflammatory anterior chamber or vitreous reaction was reported. (Fig. 2)

Discussion

Of 40 penicillin allergic patients having received an intracameral cefuroxime injection, two presented a potentially allergic conjunctival reaction. No major general or intraocular allergy was reported in our study.

Four patients of the study had their postoperative control by their usual ophthalmologist and were not examined the day after surgery in our center. Those patients did not present any immediate anaphylactic reaction in the operating theater after the injection. They are instructed to consult our emergency service if anything unusual happens during the night, and their ophthalmologists are used to send them immediately to our department if any complication or unusual feature appeared. So, we suppose that no severe allergic reaction happened for those 4 patients. We have decided to include in this study every patient declaring a penicillin allergy, without any selection of the clinical presentation of the previous reaction. Thus, we have probably included some patients with no actual penicillin allergy. But in our clinical practice, every such patient is considered as penicillin allergic and does not receive any cefuroxime. Given the wide spectrum of symptoms associated with drug allergy, the diagnosis can be challenging. According to literature, more than 80% of the presumed penicillin allergic patients would have no actual allergy [8,9]. In our study, 95.3% of the cefuroxime preoperative tests were negative (41 of 43). Montan et al. [10] reported a low cefuroxime hypersensitivity rate with only 3 positive skin prick-tests over 5813 screened patients. In the same way, it is estimated that 90% of the presumed allergic patients would have a negative penicillin skin-test [11] and can safely receive penicillin, cephalosporin and other beta-lactam agents.

The skin-test is a good predictor of tolerance [12] with a 96 to 99% sensitivity [8]. This test with a subcutaneous injection has been chosen in our protocol because the
arrangement of the operating room plans a special time for the anesthesiologist before the surgery. It can obviously be different in some departments using preferentially a topical anesthesia. It has been possible also because the pharmacy of the hospital provided ready-to-use cefuroxime syringes.

The estimation of the risk of cross-reactivity between penicillin and cephalosporin is highly variable depending on the different studies. Historically, it has been considered as 10 to 15%, but that proportion has been questioned lately. Before 1980, cephalosporins were contaminated with traces of penicillin, which has lead to an overestimation of the cross-reactivity risk [13]. Kelkar and Li [14] estimated that the risk of cross allergy is of 4.4% in case of a positive penicillin skin test and of 0.6% if the skin test is negative. Overall, according a review of literature, the cross allergy probability would be of 0.17 to 8.4% if a previous history of penicillin allergy is present, and of 0.4 to 1.9% without any penicillin allergy history [13].

The risk is not the same for every cephalosporin agent. It is related to the R1 side chain of the molecule and is more important for first generation cephalosporin than for second and third generation. The odds ratio for second generation cephalosporin such as cefuroxime is 1.1, confidence interval 0.6–2.1. Furthermore, some second-generation cephalosporins share a common R1 side chain with penicillin, so they are more likely to cross-react than others (i.e., cefaclor, cefadroxil, cefixime, cefprozil, cephalaxin, and cephradine). Cefuroxime is not one of them and the risk is considered negligible [15].

As for practical considerations, some authors recommend to avoid cephalosporin administration if any history of severe anaphylactic reaction exists [8,14,16], while others estimate that a negative skin test allows to prescribe safely cephalosporins of second and third generations [11].

Regarding cataract surgery, 67% of surgeons in United Kingdom are using cefuroxime even with documented penicillin allergy [17]. In 2006 already, Mitra et al. [18] observed that a subconjunctival cefuroxime injection was well-tolerated in penicillin allergic patients. For Myneni et al. [19], since 2010, only cephalosporin allergy is a contra-indication for cefuroxime intracameral injection. No allergic reaction is reported in their survey, neither in other large series [1,3]. Intracameral injection of cefuroxime seems possible safely, at least without previous history of severe life-threatening reaction such as anaphylactic shock, Stevens-Johnson syndrome or angioedema [16]. Statistically, the risk for endophthalmitis is greater than that for anaphylaxis, but anaphylaxis is a life-threatening event. Surgeons have to be aware of this risk, moreover when no anesthesiologist is routinely present in the operating room. If any doubt, a preliminary skin test with penicillin and/or cephalosporin can be performed for more safety. Preoperative screening is indeed one of the possible options for more safety [5], but may be expensive and cumbersome. Another solution would be the use of a different antibiotics agent, such as a fourth generation fluoroquinolone. Moxifloxacin is already currently used in some European countries [4], whereas others consider that fluoroquinolones should be reserved for curative treatment.

**Conclusion**

Intracameral injection of cefuroxime during cataract surgery seems to be well-tolerated by penicillin allergic patients with a negative preoperative subcutaneous test. For greater safety, it is recommended to select the patients according to the severity of the previous reported allergic
reaction, in order to exclude the patients with history of life-threatening manifestations. The conjunctival reactions reported in our study are acceptable towards the prevention of postoperative endophthalmitis.

Disclosure of interest

The authors declare that they have no conflict of interest concerning this article.

References