

Prophylactic Subconjunctival Cefuroxime During Cataract Surgery in Patients With a Penicillin Allergy

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ABSTRACT

The incidence of cross-reaction after subconjunctival cefuroxime following cataract surgery in penicillin allergy patients is not common and therefore cefuroxime with its better spectrum of action and lower toxicity is probably a better choice than gentamycin.

INTRODUCTION

Subconjunctival antibiotics are routinely given in the UK as prophylaxis against endophthalmitis after cataract surgery. Although cross-reactivity against cephalosporins occurs in patients allergic to penicillin, little has been documented regarding the use of subconjunctival cefuroxime, which is widely given as first line prophylaxis following cataract surgery. This article aims to identify patients with a known penicillin allergy who routinely receive subconjunctival injection of cefuroxime following cataract surgery and to assess any adverse reaction.

MATERIALS AND METHODS

Thirty-six patients having penicillin allergy preoperatively, were identified from the penicillin allergy register. All patients had undergone cataract surgery, with routine preoperative subconjunctival injection of cefuroxime. Their records were assessed retrospectively, for evidence of an adverse reaction. All patients received 125 mg of cefuroxime and 4 mg of betamethasone. Twenty-eight patients were female, seven male. The average age was 73 years (range 36–98 years). Patients who reported a penicillin allergy at preoperative assessment were included in the study. There were no exclusion criteria. Any adverse reaction, systemic or local was taken into account.

REPRINTS

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DISCLOSURE

The authors have stated that they do not have a significant financial interest or other relationship with any product manufacturer or provider of services discussed in this article. The authors also do not discuss the use of off-label products, which includes unlabeled, unapproved, or investigative products or devices.

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RESULTS

Of the 36 patients with known history of penicillin allergy, 15 had a history of a rash associated with previous penicillin treatment. Of these, one patient had also reported a possible associated loss of consciousness while another developed puffiness of the face. Three patients had a history of facial swelling and one had tongue bleeding. Following subconjunctival injection of cefuroxime, no patients were documented as having a systemic or local adverse reaction. None of the patients complained of any excessive post-operative discomfort, or more than normal eyelid or conjunctival reaction.

DISCUSSION

Endophthalmitis is a devastating complication of cataract surgery. Over the last 10 to 15 years, subconjunctival injections of prophylactic antibiotics have become commonplace following intraocular surgery. Cefuroxime is routinely used subconjunctivally after cataract surgery in conjunction with a steroid. To date, little has been documented regarding the use of subconjunctival cefuroxime in patients with penicillin allergy.

Staphylococci are the organisms most frequently responsible for producing postoperative endophthalmitis. Other causative organisms include: Gram-negative bacilli, such as *Pseudomonas* and coagulase-negative cocci. Prophylactic antibiotics should therefore be primarily effective against Gram-positive organisms. Some surgeons prefer to use subconjunctival injection of gentamycin, in cases of penicillin allergy. However, subconjunctival cefuroxime following cataract surgery causes less conjunctival toxicity, less discomfort, and possibly leaves a whiter eye than does gentamycin (1). In addition, cephalosporins achieve a much higher aqueous concentration than gentamycin at conventional doses (1). Although gentamycin may be more effective against Gram-negative bacteria, such as *Pseudomonas*, than cefuroxime, it is apparent that subconjunctival gentamycin would be a poor choice to prevent or treat endophthalmitis caused by *Staphylococcus epidermidis* and Streptococci, which accounts for over 16 times as many cases as *Pseudomonas* (1).

Although cross-reactivity of systemically administered penicillin and cephalosporin has been well established, none of the patients receiving cefuroxime, in our study, had any adverse reaction. Cassady et al. (2) reviewed 52 patients who were allergic to penicillin and subsequently received subconjunctival penicillin injection. No patients developed immediate hypersensitivity to the drug. Only 11.5% of patients reported an abnor-

mal reaction in the form of either allergic blepharitis or hives and none had a severe ocular reaction.

Penicillins contain a bicyclic nucleus, which includes the β -lactam ring and a thiazolidine ring. Cephalosporins also contain a β -lactam ring, but a dihydrothiazine ring replaces the thiazolidine ring in the bicyclic nucleus. Early case reports demonstrated a high incidence of in vitro cross-reactivity (up to 20%) between penicillins and cephalosporins (3). Cephalosporins involved in these reports included cephalothin and cephaloridine. Both agents are first-generation cephalosporins and have side chains similar to those of benzyl-penicillin, which may explain the high incidence of cross-reactivity. However, at the time of these early studies, formulations of cephalothin and cephaloridine contained trace amounts of penicillin (3). Petz et al. demonstrated a fourfold increase in the incidence of cephalosporin reactivity, including cephaloridine, cephalothin, and cephalexin, in patients allergic to penicillins (8.1%) compared with patients not allergic to penicillins (1.9%) (4). When this incidence is compared with the overall incidence of allergic reactions to cephalosporins (4%), there is a twofold increase of reactivity in patients allergic to penicillins (3). The high in-vitro cross-reactivity with penicillins and cephalosporins does not correlate with in vivo reactivity (5). Of 94 patients with positive penicillin skin tests who were subsequently administered a cephalosporin, only one patient experienced cross-reactivity manifested by bronchospasm and urticaria (5). Clinical studies of the cephalosporins indicated that patients with a history of penicillin allergy have increased incidence of reactivity to cephalosporins, but it is impossible to determine to what extent this finding is caused by immunological cross-reactivity because penicillin-allergic patients have an increased incidence of hypersensitivity reactions to drugs immunologically unrelated to penicillins (4). In addition, there is evidence of specific immune response to cephalosporins that indicates independently acquired hypersensitivity rather than cross-reactivity in some patients (4).

Periocular drug delivery using subconjunctival injections is an effective route for delivering drugs to the posterior tissues of the eye. This approach to drug delivery is safer and less invasive than intravitreal injection and also offers the exciting potential for localized, sustained-release drug delivery (6). After a subconjunctival injection, the major portion of the instilled dose is absorbed systemically through the conjunctiva, through the highly vascular conjunctival stroma and through the lid margin vessels. Significant systemic absorption also occurs when the solution enters the nasolacrimal duct and is

absorbed by the nasal and nasopharyngeal mucosa. From the systemic circulation, a major portion of the drug enters the aqueous and the vitreous. Barza et al. reported that the mean peak serum concentrations one hour after a single subconjunctival injection in animals with normal eyes ranged from 66 mg/L for ceftriaxone to 21 ± 8 mg/L for ceftizoxime (7). They also found that the peak concentration in the cornea after a single subconjunctival injection of 100 mg of ceftizoxime, cefepime, ceftazidime and ceftriaxone ranged from 400 to 3000 mg/L. Concentrations in the aqueous was about fourfold lower than those in the cornea, while that in the vitreous ranged from 13 mg/L for cefepime to 3 mg/L for ceftriaxone.

Cefuroxime being a second-generation cephalosporin, the incidence of cross-reactivity is less than a first-generation cephalosporin. It may be postulated that the amount of cefuroxime entering the systemic circulation is perhaps insufficient to cause a major systemic hypersensitivity reaction. In addition, the co-administration of subconjunctival steroid may also play a role in dampening any allergic reaction.

This study suggests that cross reaction of subconjunctival penicillin and cefuroxime is not common, but larger patient numbers need to be assessed to quantify risk more fully. Cefuroxime with its superior spectrum of action and lower toxicity is a good choice for antibiotic prophylaxis in cataract surgery.

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