ABSTRACT

Purpose: To present the outcomes of prophylaxis of postoperative endophthalmitis following cataract surgery with intracameral Cefuroxime.

Method: A retrospective study was done on 4281 eyes that underwent cataract surgery from October 2003 to September 2008. All patients underwent phacoemulsification cataract surgery. All cases received an injection of 0.1 ml intracameral Cefuroxime (1 mg) at the end of surgery except those patients allergic to penicillin and cephalosporin until September 2007 and thereafter only those with demonstrated allergy to cefuroxime.

Results: The rate of postoperative endophthalmitis was 0.11% (5 cases). Four of them had a positive culture. We found no evidence of clinical ocular toxicity.

Conclusions: Intracameral cefuroxime works very well for reducing the incidence of postoperative endophthalmitis. It appears safe to use and is easy to prepare (Arch Soc Esp Oftalmol 2009; 84: 85-90).

Key words: Postoperative endophthalmitis, cataract, phacoemulsification, cefuroxime, prophylaxis.

RESUMEN

Propósito: Mostrar los resultados de la profilaxis de endoftalmitis postquirúrgica (EPQ) tras cirugía de catarata con Cefuroxima intracamerular.

Método: Se realizó un estudio retrospectivo con 4.281 ojos intervenidos de catarata de octubre de 2003 a septiembre de 2008. Todos los pacientes fueron intervenidos con técnica de facoemulsificación. Todos los casos recibieron una inyección de Cefuroxima: 0,1 ml (1 mg) en cámara anterior al finalizar la cirugía, a excepción de los pacientes con alergia a penicilinas y cefalosporinas hasta septiembre de 2007 y después de esta fecha solo aquellos con alergia demostrada a cefuroxima.

Resultados: La incidencia de EPQ fue de 0,11% (5 casos). Cuatro de ellos fueron cultivo positivo. No se detectó ningún signo clínico de toxicidad ocular.

Conclusiones: La profilaxis de EPQ con Cefuroxima intracamerular es muy eficaz para reducir la incidencia de endoftalmitis postoperatoria, parece segura y es fácil de preparar.

Palabras clave: Endoftalmitis postquirúrgica, catarata, facoemulsificación, cefuroxima, profilaxis.
INTRODUCTION

Postoperative endophthalmitis (POE) is a serious complication of intraocular surgery. According to the series, the prevalence varies from 0.07% to 0.5% (1). Cataract surgery is the most prevalent in our environment, for which POE is the most frequent after cataract surgery. The phacoemulsification technique, with the resulting reduction in incision size and the use of intraocular lenses made with more biocompatible materials does not diminish the prevalence of this complication.

The Endophthalmitis Vitrectomy Study (EVS) (2) reported that only 69.3% of the cultures were positive after taking the aqueous and vitreous samples. The bacteria belong to the flora of the periocular tissues, mainly Staphylococcus sp coagulase negative in 70%, Staphylococcus aureus in 10%, Streptococcus sp in 9%, Enterococcus in 2%, other Gram positive species in 3%, and species Gram negative in 6%.

Although the majority of publications refer to isolated cases, grouped cases have also been described that appear in limited time and the origin is nearly always easily identifiable: solutions, intraocular lenses, viscoelastic or contaminated eye drops. However, the appearance of cases over a long period is a very complex situation and the most worrying for the Ophthalmology service.

There have been numerous perioperative measures that have tried to reduce the frequency of POE, among which we can highlight the use of antiseptics on the ocular surface, the instillation of antibiotic eye drops days before or at the start of surgery and in the postoperative, antibiotics by systemic way before surgery, antibiotic therapy in the serum for intraocular irrigation during the phacoemulsification and the irrigation/aspiration (I/A) of masses or even the use of subconjuntival antibiotics at the end of surgery. In 2002 Ciulla et al. (3) carried out an exhaustive examination of the bibliography published until now where it was seen that only the instillation of iodine povidona to 5% on the ocular surface during the three minutes before surgery was enough scientific evidence to constitute a clinical recommendation (B degree). In this way, in order to reduce the risk of POE and following the principles of evidence based medicine, as well as meticulous precautions in the cleaning and sterilizing of instruments, only the instillation of iodine povidona in the ocular surface could be advised.

The objective of this work is to present our experience of 5 years using intracamerular Cefuroxime as a prophylactic method of POE after phacoemulsification of the cataract.

SUBJECTS, MATERIAL AND MÉTHODS

It is a retrospective study of 5 years (60 months) in which 4,281 eyes were operated on for cataracts with the phacoemulsification technique and intraocular lens implant. The inclusion criteria was cataract surgery carried out by means of phacoemulsification (without combining another procedure) and intraocular lens implant, with or without posterior integral capsule. The exclusion criteria were a history of allergy to betalactams or cephalosporins until September 2007, and then only those with allergy to cefuroxime.

With patients who presented a history of allergy to Penicillin we carried out a prophylaxis with an antibiotic of Gramicidin, Neomicin and Polimixin B, a drop four times a day, three days before surgery (including the day of surgery). After September 2007 all the patients with a history of allergy to Penicillin had allergic tests Cefuroxim carried out with the above-mentioned antibiotic in more than 85% of them. When the allergy to Cefuroxim was confirmed the above-mentioned protocol was employed.

To the patients who complied with the inclusion criteria a solution of Cefuroxim was administered in the anterior chamber through the auxiliary pathway as the last surgical step.

A post operative topical prophylactic antibiotic was carried out on all the patients with a solution of Neomicine sulphate, Polimixine B sulphate and Dexametasona (with the exception of the presence of allergy to any of those components): a drop every three hours for a week and then every six hours for the other week. From January 2006 this prophylaxis was carried out with a solution of Tobramicine and Dexametasona (with the exception of the presence of allergy to any of these components).

The volume of the solution of Cefuroxim that contains 1 mg of antibiotic is 0.1 ml. The preparation of the antibiotic is carried out in the Pharmacy Service of the centre, where the sterility conditions in the laminar flow chamber are suitable.

The preparation was obtained by dissolving 250 mg of Cefuroxim in 2.5 ml of saline drip (0.9% of
ClNa). The concentration of this dissolution is 100 mg/ml. After extracting 1 ml, the rest of this solution could be stored in the refrigerator to be used in the afternoon session. One ml of the previous solution is dissolved with 9 ml of saline drip (0.9% of ClNa) achieving a concentration of 10 mg/ml. This solution is stable for around 5 hours at room temperature. For each surgery we extracted 0.1 ml in a syringe containing 1 mg of Cefuroxim. Then it was injected into the interior of the anterior chamber (4). The injection was carried as the last step of surgery with a roma cannula of the anterior chamber by means of the support incision. Carrying out the injection with a non-overdistended chamber is recommended to avoid oozing.

The diagnostic criteria for suspicion of POE were clinical: non expected intraocular inflammation in the post-operative and vitreous echoes in ultrasound A and B. The absence of pain does not rule out suspicion.

**RESULTS**

The prevalence of POE before beginning prophylaxis with intracamerular Cefuroxim was 0.5%.

All the intervened cataracts during the study time complied with the inclusion criteria for using intracameral Cefuroxime (4,281 eyes).

The prevalence of POE during the 60 months of the study was 0.11% (5 cases). None of the five cases suffered any surgical complications. Four of the cases had a positive culture. The isolated bacteria were **Pseudomona aeruginosa** resistant to Cefuroxime, **E. Coli** sensitive to Cefuroxime, the third case was reported as a possible contamination by **Corynebacterium sp** and the two remaining cases appeared in two patients with clinical histories of allergy to Penicillin to which the prophylaxis with Cefuroxime were treated with vitrectomy pars plana 20 G and intravitreous antibiotics: **Vancomicine** (1 mg in 0.1 ml) and **Amikacine** (0.4 mg in 0.1 ml) using intravitreous Triamcinolone (4 mg in 0.1 ml) in one case. The final visual acuity was 0.5 and 0.8.

Due to the fact that the last cases of POE were produced in patients with a clinical history of allergy to Penicillin it was decided to carry out on all patients having this clinical background allergy to Cefuroxime tests since in 85% of the patients with proven allergy to Penicillin no allergy to Cefuroxime was found. In fact, those two patients who had allergy to Cefuroxime, tests carried out for the intervention on the second eye were negative.

We did not observe any anterior toxic segment syndrome or edema corneal on discharge (between 1 and 1.5 months). The number of cases of cystic macular edema with visual repercussion did not seem to increase either, although we do not have the figures for prevalence before and after using prophylaxis with Cefuroxim.

Thus, the prevalence went from 0.5% to 0.11%. The calculations of the Absolute Risk Reduction (ARR), Risk Reason (RR) and the Relative Risk Reduction (RRR) were carried out. We obtained an Absolute Risk Reduction of 0.39; that is to say, the prophylaxis with intracameral Cefuroxime reduced the total prevalence of endophthalmitis. The Risk Ratio was 0.22 and the Relative Risk Reduction was 0.78, which indicates that the prophylaxis with intracameral Cefuroxime reduced the 78% prevalence of endophthalmitis after cataract surgery.

**DISCUSSION**

Before including the use of Cefuroxime, the surgical protocol of our centre for cataract surgery included the following preventive measures:

- For all the patients: cleaning of the eyelid skin with iodine povidona, instillation of 5% iodine...
povidona on the ocular surface, and rigorous sterility measures including a monitored protocol for cleaning the phacoemulsificator and I/A pieces. This protocol was carried out on each patient and filed in the Preventive medicine Service. Also, postoperative topical antibiotherapy with the previously mentioned solutions was carried out.

- For patients considered at risk (patients with diabetes mellitus, chronic obstructive bronchial pneumopathy, and local conditions that favored infection such as blepharitis or epiphora through pervious pathway) the use of topical antibiotics (combination of Gramicidine, Neomicine and Polimixine B) were added to previous measures three days after surgery.

Despite this, in our service a prevalence of 0.5% was registered. This led us to search for an additional prevention measure choosing intracamerular cefuroxime although its efficacy was still not fully endorsed in 2003. The decision to apply the intracameral cefuroxime was based on:

- The good results, security and absence of adverse effects found in the works of Montan et al (4,5).
- The opinion that probably would have a minor appearance of bacterial resistances attributable to this preventive measure in comparison with the use of other alternatives based on the use of antibiotics. It seems reasonable to think that a single dose of antibiotic in the anterior chamber, with the surgery finished and the wound closed, would not have any effect on the appearance of resistances in bacterial flora of the ocular surface and the palpebral edge. In any case, the effect should be less than the use of topical antibiotics in the irrigation saline solution during surgery or the use of topical antibiotics or perioperative subconjuntivals. The circumstances that could promote the development of bacterial resistances to an antibiotic include: intensive care units, prolonged systemic therapies and sub therapeutic doses (6).
- The fact of not being a latest stage antibiotic to treat endophthalmitis.
- In addition it would involve a minimum increase of pharmaceutical expense: with one or two preparations of 250 mg of Cefuroxime, the surgical day for morning and afternoon would be covered. Also, the preparation is quick and easy. It seems to us essential that the Pharmacy Service should be in charge of preparing the dissolution of antibiotics to guarantee the conditions of dosage and sterility.

In 2006 a preliminary report of a multinational, prospective, randomized, placebo-controlled and partially masked report was published on POE prophylaxis by the European Society of Cataract and Refractive Surgery (ESCRS) (7) where the efficacy of intracameral Cefuroxim versus placebo and perioperative Levofloxacine was superior: The prevalence of POE without Cefuroxime was approximately five times greater. These results encouraged us to continue using this prophylaxis in our Service.

From September 2007 we have carried out allergy to Cefuroxim tests on all patients who had allergy to Penicillin. The fact that the two last cases of endophthalmitis were produced on two patients where the aforementioned prophylaxis for this background was not carried out made us raise the possibility of carrying out allergy to Cefuroxim tests. The delay this caused in the preop stage and the additional expense are small. This has also meant that practically all the patients can benefit from this prophylaxis.

In 2007 the definitive results of the trial on Prophylaxis of postoperative endophthalmitis promoted by ESCRs were published. As well as showing the efficacy of intracameral cefuroxim, some risk factors such as the incision in the clear cornea, the use of silicone lenses and the presence of surgical complications (8) were identified in the report. In our case, these factors should have little to do with the prevalence of POE in the pre and post cefuroxim stages since the type of incision was invariably in the clear cornea and the lenses implanted were of acrylic hydrophobic material. Also, none of the five cases of POE had surgical complications.

We decided to include in this prophylaxis protocol the patients that suffered fracture of the posterior capsule during surgery as we think that the risk of suffering an endophthalmitis was greater than the possible risk of retinal toxicity due to an injection of cefuroxime. In our experience, the introduction of this additional prophylactic measure has been extremely efficient since it involved a reduction in the POE prevalence of 0.5% to 0.11%. However, it is still greater than the published by the ESCRs Endophthalmitis Study Group: 0.049% (total n.º of endophthalmitis in the group with cefuroxime and preoperative topical levofloxacine) (8) and by Lundström et al: 0.048% (total n.º of endophthalmitis with prophylaxis of cefuroxime) (9). Yu-Wai-
Man et al compared the efficacy of intracamerular and subconjunctival cefuroxime obtaining a lower prevalence of endophthalmitis through the intracameral path: 0.046% (10).

Probably, our POE prevalence would have been less (0.07%) if we had applied intracamerular cefuroxime to the two patients with allergy to Penicillin.

On the other hand, in our experience it seems that intracameral cefuroxime is safe. Montan arrived at the same conclusion based on results he published in 2002 (5). None of the 4281 operated eyes presented corneal edema or increase of inflammation in the anterior chamber in the follow up time.

Many ophthalmologists, above all in the United States, expressed a reluctance to using intracameral antibiotics for safety and medical-legal reasons due to the absence of a commercial preparation with an approved administration pathway (11). This is a fact and it does not seem that there is a pharmaceutical company willing to manufacture it. One alternative to this prophylaxis could be the fourth generation topical kinolones (gatifloxacine and moxifloxacine); however, they are not available in Spain. Nevertheless, Cases have been published on endophthalmitis in patients where they were used as prophylaxis, even several days before surgery (12). Also, bacterial resistances to these antibiotics have been described in ocular samples (13).

As conclusions we can state that the injection of cefuroxim in the anterior chamber is a very efficient measure for the prophylaxis of POE. Its safety could be good although additional studies are necessary on this aspect. It is a simple maneuver and it does not appreciably increase the surgery time. The pharmaceutical expense that it represents is low and the preparation technique is simple.

REFERENCES