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ADIS DRUG PROFILE

Intracameral Cefuroxime

Prophylaxis of Postoperative Endophthalmitis after Cataract Surgery

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Abstract Results of the landmark European Society of Cataract and Refractive Surgeons trial and additional prospective and retrospective studies support the use of intracameral cefuroxime in the prophylaxis of endophthalmitis following cataract surgery. Prophylaxis with intracameral cefuroxime at the recommended dose appears to be well tolerated in patients undergoing cataract surgery. However, off-label use of intracameral cefuroxime usually requires a two-step dilution process with the potential for dilution errors, and there are also concerns regarding the risk of contamination. Aprokam® (intracameral cefuroxime) has been approved in the EU for the prophylaxis of postoperative endophthalmitis after cataract surgery. After reconstitution of Aprokam®, no further dilution is required and each vial is only indicated for single-patient use; this has the potential to reduce the risk of both dilution errors and contamination.

Key features and properties of intracameral cefuroxime (Aprokam®)

Indication

Prophylaxis of postoperative endophthalmitis after cataract surgery

Dosage and administration

Approved dose	1 mg of cefuroxime (0.1 mL of the reconstituted solution)
Route of administration	Intracameral use: slowly inject 0.1 mL of the reconstituted solution into the anterior chamber of the eye at the end of surgery
Availability	Single-use vial containing 50 mg of cefuroxime powder
Reconstitution procedure	Reconstitute with 5 mL of sterile sodium chloride 0.9 % solution for injection

Pharmacokinetic properties

Systemic exposure following intracameral injection expected to be negligible

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1 Introduction

In Europe, cataract surgery is the most common surgical procedure performed in the elderly [1]. Although uncommon (occurring with an incidence of 0.05–0.3 %), endophthalmitis is a serious complication of cataract surgery and may result in severe, permanent visual loss [2]. The most common pathogens causing acute endophthalmitis following cataract

surgery include coagulase-negative staphylococci, *Staphylococcus aureus*, β-haemolytic streptococci, *Streptococcus pneumoniae*, *Streptococcus mitis*, *Enterococcus faecalis* and Gram-negative rods (including *Haemophilus influenzae* and *Pseudomonas aeruginosa*) [3]. *Propionibacterium acnes* is also implicated in chronic, postoperative endophthalmitis [3]. Particularly poor visual outcomes are usually seen in endophthalmitis associated with *Streptococcus* spp. [2].

Guidelines issued after the publication of the landmark European Society of Cataract and Refractive Surgeons (ESCRS) study (see Sect. 3), including ESCRS guidelines [3], French guidelines [4] and, depending on local endophthalmitis rates, UK guidelines [5], recommend the postoperative use of intracameral cefuroxime for the prophylaxis of endophthalmitis after cataract surgery. The advantage of intracameral injection is that a high concentration of cefuroxime in the anterior chamber is guaranteed with this route of administration [2, 6].

Although the results of the ESCRS study generally led to increased use of intracameral cefuroxime in Europe, survey results indicate reluctance on the part of some surgeons to adopt the routine use of intracameral cefuroxime [7–10]. This reluctance primarily reflects concern regarding the potential for errors during the preparation of cefuroxime solution for intracameral injection [8, 10, 11]. In particular, dilution errors may arise, given that two dilution steps are generally required to reconstitute cefuroxime sodium powder for off-label administration by intracameral injection [3, 8, 11]. Indeed, inaccurate preparation of intracameral cefuroxime has been reported [12–15], sometimes resulting in ocular toxicity (see Sect. 4) [12–14]. There has also been concern regarding the potential for bacterial contamination when several doses of cefuroxime are decanted from one vial [10, 11]. Survey results suggest that uptake of intracameral cefuroxime may increase if there was a commercially available preparation indicated for intracameral use [8, 10, 16].

Aprokam® is the first cefuroxime preparation to be approved in the EU for intracameral injection for the prophylaxis of postoperative endophthalmitis after cataract surgery [17]. Each Aprokam® vial contains 50 mg of cefuroxime powder, which is reconstituted with 5 mL of sterile sodium chloride 0.9 % solution for injection; 0.1 mL of the reconstituted solution (i.e. 1 mg of cefuroxime) is then administered to the patient by intracameral injection [17]. Thus, Aprokam® requires only one-step reconstitution, without further dilution, which has the potential to reduce the risk of preparation errors. Each vial of Aprokam® is intended for single-patient use, which reduces the risk of contamination.

This article reviews the clinical efficacy and tolerability of intracameral cefuroxime for the prophylaxis of postoperative endophthalmitis after cataract surgery, as well as summarizing its pharmacological properties. Dosage and administration recommendations for Aprokam® are also discussed.

Data sources: Medical literature (including published and unpublished data) on 'intracameral cefuroxime in patients undergoing cataract surgery' was identified by searching databases (including MEDLINE and EMBASE) for articles published since 1996 to 7 January 2013, bibliographies from published literature, clinical trial registries/databases and websites (including those of regional regulatory agencies and the manufacturer). No language restrictions were applied. Additional information (including contributory unpublished data) was also requested from the company developing the drug.

Search terms: 'Cefuroxime', 'intracameral', 'cataract' and 'endophthalmitis'.

Study selection: Studies in patients undergoing cataract surgery who received prophylaxis with intracameral cefuroxime. Inclusion of studies was based mainly on the methods section of the trials. When available, large, well controlled trials with appropriate statistical methodology were preferred. Relevant pharmacodynamic and pharmacokinetic data are also included.

Keywords: Cefuroxime, intracameral, cataract surgery, endophthalmitis, therapeutic efficacy, tolerability, pharmacodynamics, pharmacokinetics.

2 Pharmacological Properties

2.1 Mechanism of Action

The second-generation cephalosporin cefuroxime is a β-lactam antibacterial [18]. Its primary inhibitory target is penicillin-binding protein (PBP) 3, although it also inhibits PBP1a and PBP1b [18]. The inhibition of PBP by cefuroxime blocks peptidoglycan synthesis and cell wall production, eventually resulting in bacterial lysis [17, 18].

2.2 Antibacterial Activity

Cefuroxime demonstrates in vitro activity against a broad range of Gram-positive and Gram-negative bacteria, including streptococci and meticillin-sensitive *S. aureus* [18]. Cefuroxime is highly stable in the presence of β-lactamases produced by certain Gram-negative bacteria [19]. However, in keeping with other β-lactam antibacterials, cefuroxime has no activity against meticillin-resistant staphylococci; *Pseudomonas* spp. are also resistant to cefuroxime [18, 19]. Penicillin-resistant *S. pneumoniae* are

cross-resistant to cephalosporins, including cefuroxime [17]. In addition, β-lactamase-negative, ampicillin-resistant strains of *H. influenzae* should be considered resistant to cefuroxime [17].

Limited data are available from recent European studies examining the in vitro activity of cefuroxime against ocular pathogens [20–22]. It should be noted that susceptibility and/or resistance in these studies was determined using systemic breakpoints/criteria from the Clinical and Laboratory Standards Institute [20, 21] and British Society of Antimicrobial Chemotherapy [22]. These breakpoints are derived from data correlating minimum inhibitory concentrations (MICs), antibacterial plasma concentrations and clinical outcome following the systemic administration of antibacterials, and are of limited relevance to the intracameral route of administration, given the high concentrations achieved in the anterior chamber following intracameral injection.

Briefly, in conjunctival bacteria isolated from Spanish patients scheduled to undergo cataract surgery in 2006–2007, in vitro cefuroxime resistance rates were 3.2 % against streptococci ($n = 431$ isolates), 18.6 % against *Haemophilus* spp. ($n = 70$), 5.3 % against Gram-negative cocci ($n = 76$) and 40.7 % against Gram-negative rods ($n = 59$) [20]. The in vitro sensitivity of *S. pneumoniae* ($n = 93$ isolates) isolated from Greek patients with conjunctivitis or keratitis to cefuroxime remained stable between 2000–2004 (susceptibility rate of 83.3 %) and 2005–2009 (susceptibility rate of 88.2 %) [21]. Finally, the susceptibility of *S. pneumoniae* ($n = 67$ isolates) isolated from UK patients with keratitis in 2003–2006 to cefuroxime was 98.5 % [22].

In vitro, cefuroxime significantly inhibited the adherence of *Staphylococcus epidermidis* to intraocular lenses [23, 24].

2.3 Mechanisms of Resistance

Mechanisms of cefuroxime resistance include hydrolysis by β-lactamases (including certain extended-spectrum beta-lactamases), reduced affinity of PBPs for cefuroxime, cell membrane impermeability restricting the access of cefuroxime to PBPs, and drug efflux pumps [17, 18]. However, use of intracameral cefuroxime over the past 10–15 years does not appear to have been associated with an increase in resistance among pathogens implicated in endophthalmitis [19]. Moreover, development of resistant strains is not expected to be a major issue following the administration of a single antibacterial dose that achieves high local concentrations (such as seen with intracameral cefuroxime) [19].

2.4 Effects on Ocular Tissues

In vitro, no cytotoxic effects were seen on cultured human corneal endothelial cells at cefuroxime concentrations of $\leq$2.75 mg/mL [25]. Significant ($p < 0.05$), dose-dependent reductions in the number of viable cells was seen at cefuroxime concentrations of $\geq$5 mg/mL [25].

No significant change in corneal thickness and no anterior chamber reaction was seen following administration of intracameral cefuroxime 1 mg to rabbits [26]. However, corneal levels of malondialdehyde (a marker of oxidative stress) significantly ($p < 0.001$ vs. controls) increased and those of total thiol (an antioxidant marker) significantly ($p = 0.001$ vs. controls) decreased with intracameral cefuroxime [26].

Intravitreal injection of cefuroxime 1 mg was not associated with functional or histological retinal damage in rabbits [27]. However, intravitreal cefuroxime 10 mg was associated with retinal toxicity, including reduced electroretinogram responses and marked histological damage [27].

Studies examining the effects of intracameral cefuroxime on ocular tissues in patients undergoing cataract surgery are discussed in Sect. 4.

2.5 Pharmacokinetic Profile

Systemic exposure following the intracameral injection of cefuroxime is expected to be negligible [17]. Following intracameral injection of cefuroxime 1 mg in patients undergoing cataract surgery, the mean intracameral cefuroxime concentration was 2,614 mg/L 30 s postoperatively and 1,027 mg/L 1 h postoperatively, with median values of 2,742 and 756 mg/L at the corresponding time points [28]. By contrast, 12–24 min after subconjunctival injection of cefuroxime 25 mg, the mean aqueous cefuroxime concentration was only 2.31 mg/L in patients undergoing cataract surgery [29].

Systemic interactions with other drugs are considered unlikely, given that negligible systemic exposure is seen with the use of intracameral cefuroxime [17].

2.6 Pharmacodynamic/Pharmacokinetic Relationship

For cephalosporins, the most important pharmacodynamic/pharmacokinetic parameter, in terms of predicting clinical efficacy, is the percentage of the dosing interval for which the drug concentration is above the MIC for a given pathogen [18]. The cefuroxime concentration in the aqueous humour exceeded the MIC of several relevant pathogens for up to 4–5 h after surgery in patients receiving intracameral cefuroxime 1 mg [17].

3 Therapeutic Efficacy

This section summarizes the results of studies examining the efficacy of off-label intracameral cefuroxime in the prophylaxis of endophthalmitis in patients undergoing cataract surgery. The efficacy of intracameral cefuroxime was initially shown in observational [30] and retrospective [31] studies, which were followed by the landmark ESCRS study [32]. Subsequent analyses have confirmed the efficacy of intracameral cefuroxime [16, 33–40]. Several of these studies were used to support the approval of the Aprokam® formulation of intracameral cefuroxime, given that there are no therapeutic efficacy data specifically relating to Aprokam®.

3.1 The ESCRS Study

The randomized, multinational ESCRS study examined the efficacy of intracameral cefuroxime and levofloxacin 0.5 % ophthalmic solution as prophylaxis against endophthalmitis in patients undergoing phacoemulsification cataract surgery with intraocular lens implantation [32]. The ESCRS study used a two-by-two factorial design. In terms of perioperative antibacterial prophylaxis, patients received intracameral cefuroxime 1 mg, levofloxacin 0.5 % ophthalmic solution, intracameral cefuroxime 1 mg plus levofloxacin 0.5 % ophthalmic solution or no prophylaxis (see Table 1 for further details). Prior to surgery, all patients received topical povidone/iodine 5 % drops (administered into the conjunctival sac and onto the cornea for ≥3 min prior to surgery). Starting the day after surgery, all patients were instructed to use levofloxacin 0.5 % ophthalmic solution four times daily for 6 days [32]. It should be noted that the ESCRS study has been subject to several criticisms, including the lack of a subconjunctival cefuroxime treatment arm [9]. It has also been suggested that a fourth-generation fluoroquinolone would have been a more appropriate comparator than levofloxacin [19].

The primary endpoints were the incidence of total endophthalmitis and the incidence of proven endophthalmitis [1]. The ESCRS study was terminated prematurely because of positive interim results [41].

In the final analysis of the intent-to-treat population, the risk of total endophthalmitis was approximately fivefold higher and that of proven endophthalmitis was approximately sixfold higher in patients not receiving intracameral cefuroxime than in those receiving intracameral cefuroxime (Table 1) [32]. By contrast, the risk of total endophthalmitis and proven endophthalmitis did not significantly differ between patients not receiving levofloxacin 0.5 % ophthalmic solution and those who did receive levofloxacin 0.5 % ophthalmic solution (Table 1). Similar findings were seen in the per-protocol population [32].

Visual acuity (assessed between 3 weeks and 8 months after initial presentation) was 20/80, 20/60 and 20/25 in the three patients with endophthalmitis who had received intracameral cefuroxime alone and 20/80 and 20/25 in the two patients with endophthalmitis who had received intracameral cefuroxime plus levofloxacin 0.5 % ophthalmic solution [42]. Visual acuity ranged between <20/200 and 20/25 in the ten patients who had received levofloxacin 0.5 % ophthalmic solution alone and developed endophthalmitis and the 14 patients who had received no prophylaxis and developed endophthalmitis [42].

In the 20 cases of proven endophthalmitis, the microorganisms isolated were *S. epidermidis* ($n = 2$ cases) in patients receiving intracameral cefuroxime alone; *S. aureus* ($n = 1$), *S. epidermidis* ($n = 2$), *Staphylococcus hominis*/*Staphylococcus haemolyticus* ($n = 1$), *Streptococcus salivarius* ($n = 1$), *Streptococcus sanguinis* ($n = 1$) or *Streptococcus oralis* ($n = 1$) in patients receiving levofloxacin 0.5 % ophthalmic solution alone; *Staphylococcus warneri* ($n = 1$) in patients receiving intracameral cefuroxime plus levofloxacin 0.5 % ophthalmic solution; and *S. epidermidis* ($n = 3$), *S. epidermidis*/*S. mitis* ($n = 1$), *S. aureus*/*P. acnes* ($n = 1$), *P. acnes* ($n = 1$), *S. pneumoniae* ($n = 2$), *S. salivarius* ($n = 1$) and *Streptococcus suis* ($n = 1$) in patients receiving no prophylaxis [42]. Visual outcomes were worse in patients with streptococcal infection than in those with staphylococcal infection; however, no cases of streptococcal endophthalmitis were seen in patients receiving intracameral cefuroxime [42].

The onset of endophthalmitis occurred within 5–13 days among patients receiving intracameral cefuroxime alone, 4 days among patients receiving intracameral cefuroxime plus levofloxacin 0.5 % ophthalmic solution, 1–9 days among patients receiving levofloxacin 0.5 % ophthalmic solution alone, and 2–132 days among patients receiving no prophylaxis [42].

3.2 Additional Studies

Results of additional studies examining the efficacy of intracameral cefuroxime in the prophylaxis of endophthalmitis after cataract surgery support the findings of the ESCRS study [16, 30, 31, 33–40]. Most of these additional studies were European [30, 31, 33–38, 40], with one conducted in the USA [39] and one conducted in South Africa [16]. Where specified, these multicentre [30, 35, 38, 39] or single-centre [16, 31, 33, 34, 36, 40] studies were of prospective observational [30, 33–35] or retrospective [31, 36, 38–40] design.

In two large, prospective, Swedish studies, the incidence of endophthalmitis was significantly lower in patients receiving intracameral cefuroxime than in patients not receiving intracameral cefuroxime within the same time

Table 1 Efficacy of intracameral cefuroxime for the prophylaxis of postoperative endophthalmitis after cataract surgery. Primary endpoint results of the ESCRS study [32]

Treatment[a]	No. of ITT pts	Incidence of total endophthalmitis (% of pts)[b]	Incidence of proven endophthalmitis (% of pts)[c]
IC CXM + PL	4,056	0.074	0.049
IC CXM + LVX	4,052	0.049	0.025
No IC CXM + LVX	4,049	0.247	0.173
No IC CXM + PL	4,054	0.345	0.247

IC CXM intracameral cefuroxime, *ITT* intent to treat, *LVX* levofloxacin 0.5 % ophthalmic solution, *PL* placebo eye drops, *pts* patients

[a] In this study with a two-by-two factorial design, administration of LVX, but not IC CXM, was masked. Pts received five drops of LVX or PL (one drop 1 h before surgery, one drop 30 min before surgery and three drops at 5-min intervals starting immediately after surgery), or IC CXM 1 mg injected into the anterior chamber at the end of surgery

[b] The odds ratio for total endophthalmitis in pts receiving no IC CXM (i.e. no IC CXM + LVX and no IC CXM + PL) versus IC CXM (i.e. IC CXM + PL and IC CXM + LVX) was 4.92 (95 % CI 1.87–12.9) [$p = 0.001$] and in pts receiving no LVX (IC CXM + PL and no IC CXM + PL) versus LVX (no IC CXM + LVX and IC CXM + LVX) was 1.41 (95 % CI 0.67–2.95)

[c] The odds ratio for proven endophthalmitis in pts receiving no IC CXM (i.e. no IC CXM + LVX and no IC CXM + PL) versus IC CXM (i.e. IC CXM + PL and IC CXM + LVX) was 5.86 (95 % CI 1.72–20.0) [$p = 0.005$] and in pts receiving no LVX (IC CXM + PL and no IC CXM + PL) versus LVX (no IC CXM + LVX and IC CXM + LVX) was 1.51 (95 % CI 0.62–3.7)

period (0.045 vs. 0.350 % [35] and 0.053 vs. 0.220 % [30]) (Table 2).

Four other studies reported a significantly lower incidence of endophthalmitis after versus before the introduction of routine prophylaxis with intracameral cefuroxime (0.043–0.08 vs. 0.26–1.238 %) [16, 31, 33, 34], with no significant difference seen before and after the introduction of intracameral cefuroxime in a fifth study [37] (Table 2). A decline in the incidence of endophthalmitis was also seen in a US study after the introduction of intracameral antibacterial prophylaxis (intracameral cefuroxime was used in the vast majority of cases) (Table 2) [39]. In this study, a subgroup of patients ($n = 2{,}038$) without posterior capsule rupture received intracameral antibacterials alone (i.e. without postoperative topical antibacterials) between 2008 and 2011; the incidence of endophthalmitis in these patients was 0.049 % [39].

Another retrospective study reported a significantly lower incidence of endophthalmitis with intracameral cefuroxime than with subconjunctival injection of cefuroxime (0.046 vs. 0.139 %) (Table 2) [40].

Low rates of endophthalmitis in patients receiving intracameral cefuroxime were also reported in two other retrospective analyses (Table 2) [36, 38].

4 Safety and Tolerability

Prophylaxis with intracameral cefuroxime at the recommended dose appears to be well tolerated in patients undergoing cataract surgery. Over 450,000 patients were exposed to intracameral cefuroxime in the clinical trials discussed in Sect. 3. Although most of the clinical trials did not specifically discuss adverse events, one of the retrospective analyses reported no cases of anterior toxic segment syndrome or corneal oedema in patients receiving intracameral cefuroxime [36].

The EU summary of product characteristics states that no particular adverse effects have been reported in the literature in patients receiving intraocular injection of cefuroxime, apart from very rare cases of anaphylactic reaction (<1 in 10,000 patients) [17], including in a patient with known penicillin allergy [43].

Several small studies found no ocular toxicity in cataract surgery patients receiving the recommended dose of intracameral cefuroxime 1 mg [28, 44, 45]. For example, there were no significant differences between patients undergoing cataract surgery who received intracameral cefuroxime 1 mg ($n = 45$) and those who did not ($n = 45$) in terms of induced laser flare changes at 1 day, 3 days or 3 months postoperatively, changes in endothelial cell count at 3 months postoperatively, or visual acuity at 3 months postoperatively, according to the results of a randomized, observer-masked, single-centre study [28].

Five weeks after undergoing cataract surgery, neither the central nor the entire mean macular thickness significantly differed between patients receiving intracameral cefuroxime 1 mg ($n = 23$) and patients receiving intracameral balanced salt solution ($n = 17$), according to the results of a randomized, double-masked, single-centre study [44].

In addition, among patients who did ($n = 128$) and did not ($n = 128$) receive intracameral cefuroxime 1 mg following cataract surgery, average endothelial cell loss was 26 % and 32 % in the corresponding treatment groups 1 month after surgery, average macular thickness increased by 7.6 % in both treatment groups and the increase in best-corrected visual acuity did not differ between the treatment groups, according to the results of a nonrandomized, single-centre study (available as an abstract) [45].

Table 2 Efficacy of intracameral cefuroxime for the prophylaxis of postoperative endophthalmitis after cataract surgery

Study (country)	Treatment[a] (year)	No. of pts	Postoperative endophthalmitis	
			Incidence (% of pts)	OR/RR/RRR (95 % CI)
Prospective observational studies				
Barreau et al. [33][b] (France)	IC CXM (2006–2008)	2,289	0.044***	
	Prior to IC CXM (2003–2006)	2,826	1.238	OR 28.998 (4.0–211.9)
García-Sáenz et al. [34][b] (Spain)	IC CXM (2005–2008)	7,057	0.043*	RR 0.072 (0.022–0.231)
	Prior to IC CXM (1999–2005)	6,595	0.590	
Lundström et al. [35][c] (Sweden)	IC CXM (2002–2004)	223,156	0.045***	
	No IC CXM (2002–2004)	2,315	0.350	OR 7.236 (3.71–14.11)
Wejde et al. [30][c] (Sweden)	IC CXM (1999–2001)	151,874	0.053***	
	No IC CXM (1999–2001)	6,805	0.220	OR 3.649 (2.291–5.812)
Retrospective studies				
Diez et al. [36][b] (Spain)	IC CXM (2003–2008)	4,281	0.11	RRR 78 %
	Prior to IC CXM (NR)	NR	0.5	
Fontanet et al. [37][b,d] (Spain)	IC CXM (2007–2008)	2,078	0.048	OR 0.396 (0.049–3.167)
	Prior to IC CXM (2003–2007)	6,586	0.121	
Gualino et al. [38] (France)	IC CXM (2007–2008)	3,316	0.06	
Montan et al. [31][b] (Sweden)	IC CXM (1996–2000)	32,180	0.06***	
	Prior to IC CXM (1990–1995)	34,102	0.26	
Shorstein et al. [39][b,e] (USA)	IC CXM (2008–2009)	6,278	0.143	
	IC CXM, MXF or VAN (2010–2011)	7,108	0.014	
	Prior to IC CXM (2007)	2,878	0.313	
van der Merwe et al. [16][b,d] (South Africa)	IC CXM (2006–2009)	3,971	0.08**	RRR 86 % (53.9–95.8)
	Prior to IC CXM (2003–2006)	4,219	0.55	
Yu-Wai-Man et al. [40][b] (UK)	IC CXM (2003–2006)	17,318	0.046**	
	SC CXM (2000–2003)	19,425	0.139	OR 3.01 (1.37–6.63)

CXM cefuroxime, *IC* intracameral, *MXF* moxifloxacin, *NR* not reported, *OR* odds ratio, *pt(s)* patient(s), *RR* relative risk, *RRR* relative risk reduction, *SC* subconjunctival, *VAN* vancomycin

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$ versus comparator group

[a] Where specified, perioperative topical povidone/iodine [16, 33, 34, 38–40] or chlorhexidine [31] was used in all patients. Where specified, patients also received postoperative corticosteroid [33, 34, 36, 40], antibacterial [33, 34, 36, 39], NSAID [33, 34] and/or anticholinergic [33] eye drops

[b] Studies compared the endophthalmitis rate after the introduction of routine prophylaxis with IC CXM with that before the routine use of IC CXM

[c] Studies compared the endophthalmitis rate in pts receiving IC CXM with that in pts not receiving IC CXM within the same time period

[d] Not specified if this study was of retrospective or prospective design

[e] During 2008–2009, IC CXM was offered to pts unless contraindicated by allergy or posterior capsule rupture. In 2010–2011, all pts received IC antibacterials with IC CXM the first-line antibacterial, IC MXF if the pt was allergic to penicillin or cephalosporins, or IC VAN if the pt was allergic to penicillin, cephalosporins or fluoroquinolones

However, ocular toxicity was reported in cataract surgery patients receiving higher than recommended doses of intracameral cefuroxime as a result of dilution and/or administration errors [12–14]. For example, anterior segment inflammation and macular oedema with serous retinal detachment were seen in six patients who received intracameral cefuroxime 40–50 mg, although all patients had a satisfactory final visual outcome [12]. Various toxic effects (including temporary corneal oedema, temporary raised intraocular pressure, loss of corneal endothelial cells, electroretinography changes and/or permanent vision loss) were seen in 16 patients who received estimated intracameral cefuroxime doses of ≈10–100 mg [13]. In addition, macular infarction occurred in a patient who inadvertently received an intracameral cefuroxime dose of ≈62.5 mg following cataract surgery; the patient had a final pinhole visual acuity of 3/60 2 months postoperatively [14]. By contrast, no ocular toxicity was seen in six cataract surgery patients who received intracameral cefuroxime 3 mg as the result of a dilution error [15].

5 Dosage and Administration

Aprokam® must be administered by intracameral injection by an ophthalmic surgeon in the recommended aseptic conditions of cataract surgery [17]. The recommended dose of cefuroxime 1 mg (0.1 mL of reconstituted solution) should not be exceeded [17]. This is in keeping with guidelines, which recommend administration of 1 mg of intracameral cefuroxime [3, 4].

Each Aprokam® vial contains 50 mg of cefuroxime powder [17]. To reconstitute Aprokam®, 5 mL of sterile sodium chloride 0.9 % solution for injection should be injected into the Aprokam® vial. The vial should be gently shaken until the solution is free of visible particles. At least 0.1 mL of the solution should then be aspirated using a 1 mL syringe and the dose adjusted to the 0.1 mL mark on the syringe. At the end of cataract surgery, 0.1 mL of the reconstituted solution should be slowly injected into the anterior chamber of the eye. Each vial of Aprokam® is only intended for single-patient use [17].

Dosage adjustments are not needed in the elderly or in patients with renal or hepatic impairment [17]. The optimal dose and safety of Aprokam® have not been established in paediatric patients [17].

Local prescribing information should be consulted for additional information concerning contraindications, special warnings and precautions, the preparation of Aprokam® and its intracameral administration.

6 Intracameral Cefuroxime: Current Status

Intracameral cefuroxime (Aprokam®) is approved in the EU for the prophylaxis of postoperative endophthalmitis after cataract surgery [17].

Results of the ESCRS trial and additional prospective and retrospective studies support the use of intracameral cefuroxime in the prophylaxis of endophthalmitis following cataract surgery (Sect. 3). Indeed, based on the ESCRS study findings, ESCRS guidelines recommend the use of intracameral cefuroxime in this indication [3]. Intracameral cefuroxime is also recommend by French guidelines [4] and, depending on local endophthalmitis rates, UK guidelines [5].

Some surgeons have expressed reluctance to use off-label intracameral cefuroxime because of the potential for dilution errors associated with the two-step dilution process needed for reconstitution. In addition, concerns have been raised concerning the potential for contamination. By contrast, only one-step reconstitution of Aprokam® is required for reconstitution and each vial is only indicated for single-patient use; this has the potential to reduce the risk of both dilution errors and contamination [19].

In conclusion, the Aprokam® preparation of intracameral cefuroxime represents a useful advance for the prophylaxis of endophthalmitis after cataract surgery.

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