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Control of inflammation and prophylaxis of endophthalmitis after cataract surgery: A multicenter study

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PURPOSE. *To compare two different postcataract surgery antibiotic/steroid therapeutic combinations, for clinical results as well as patient satisfaction.*
METHODS. *Prospective randomized clinical trial of patients with bilateral operative cataract. Postoperatively, for 15 days one eye was randomly assigned to therapy with the combination chloramphenicol 0.25%–betamethasone 0.13% gel three times a day (Group 1) and the other to the combination tobramycin 0.3%–dexamethasone 0.1% eyedrops four times a day (Group 2).*
RESULTS. *A total of 142 patients (284 eyes) completed the study. The authors could not detect any significant difference between Group 1 and Group 2 concerning preoperative evaluation, surgical procedure, and complications. Pertaining to the two therapeutic regimens, efficacy, side effects, and clinical findings such as uncorrected visual acuity, intraocular pressure, edema or hyperemia of eyelids and/or conjunctiva, conjunctival and/or ciliary vessels congestion, decreased corneal transparency, corneal edema, Descemet folds, anterior chamber Tyndall and depth, and posterior synechiae were also comparable. Postoperative subjective pain and dry eye sensation were comparable between the two groups, while the gel preparation elicited a significantly more pleasant sensation in the patients (p=0.04).*
CONCLUSIONS. *The motivation for use of a gel is to prolong the permanence of associated drugs on the ocular surface, increasing potency and decreasing concentration of the drug and rate of administration. This in order to improve compliance and decrease potential side effects. Chloramphenicol 0.25%–betamethasone 0.13% gel combination proved to have comparable efficacy, tolerance, and better acceptance by the patients than an aqueous tobramycin 0.3%–dexamethasone 0.1% preparation. (Eur J Ophthalmol 2007; 17: 733-42)*

KEY WORDS. *Antibiotic/steroid association, Cataract surgery, Postoperative therapy*

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INTRODUCTION

Presently, cataract extraction with intraocular lens (IOL) implantation is the most frequently performed surgery in Italy, with almost 460,000 cases per year (Ministero della Salute, Repubblica Italiana. Available at: http://www.ministerosalute.it/ programmazione/sdo/ ric_informazioni/ default.jsp). Modern cataract surgery techniques, i.e., phacoemulsification with reduced use of ultrasounds, sutureless small incision, and foldable IOLs, reduced surgery-related trauma. However, postoperative inflammation remains a frequent, somewhat normal phenomenon: moderate iritis with increase of proteins and cells in the aqueous, at times with minute lens fragments (1). This complication often resolves spontaneously, but when its duration is prolonged, it may induce other complications, such as clinically detectable cystoid macular edema, inflammatory deposits or membrane on the IOL, or posterior capsule opacification (2-5). The adoption of anti-inflammatory drugs is the customary way of controlling and eliminating anterior segment inflammation in the immediate postoperative period. Furthermore, this therapy improves possible inflammation-induced symptoms (6).

A dreadful complication of cataract surgery, endophthalmitis, is much rarer, with an incidence of 0.1%, but with high frequency of severe visual reduction and possible resort to enucleation (7, 8). Even if the occurrence rate of these complications is limited, it is impossible to predict which patient will be involved, and how severely. A 0.1% prevalence of endophthalmitis would lead to 300 to 400 cases of endophthalmitis per year in Italy. For these reasons, and for legal purposes, almost all cataract surgery patients in Italy receive postoperative antibiotic/anti-inflammatory topical treatment regimen for 1 to 2 weeks after surgery.

There is no general consensus among surgeons on recommended antibiotics. A recent study by Jensen et al on almost 10,000 patients indicates more efficacy of ofloxacin when compared to ciprofloxacin. According to a recent ASCRS survey several wide-spectrum antibiotics are currently used, including ofloxacin, oxyfloxacin, gentamicin, tobramycin, and others (8, 9). This lack of consensus likely indicates an almost similar clinical efficacy, regardless of laboratory-defined spectra. The only relevant side effect after topical antibiotic administration is the occurrence of an allergic reaction, facilitated by drug concentration and frequency of administration (10).

Considering inflammation, corticosteroids have the widest range of activity, including inhibition of elaboration, release, and action of freshly produced inflammation mediators. For this reason corticosteroids are the most frequently used postoperative drugs (9). Nevertheless, the topical use of corticosteroids may lead to intraocular pressure increase, delayed wound healing, and, with very prolonged use, induction of systemic side effects (11). In order to prevent this, currently synthetic steroids with low intraocular penetration and/or systemic adsorption are used, or, as an alternative, nonsteroidal anti-inflammatory drugs (12, 13).

A possible solution for reducing the rare, but nevertheless disturbing side effects of this postoperative treatment is the reduction of concentration and frequency of administration of the involved drugs, without reduction of their efficacy. Reduction in efficacy is especially relevant when the drug is administered in a solution that immediately dissolves in the tear film, the natural protection system of the ocular surface, with intrinsic dilution properties and part of the mechanical removal system of contaminants from the ocular surface.

In order to increase the clinical efficacy/quantity of administered drug ratio, a diluent that increases the permanence time of the drug on the ocular surface can be used, with consequent reduction in half-life in ocular fluids and tissues. This possibility has been already been discussed and then confirmed by experimental and clinical studies, showing that drug administration is more efficacious in gel than in aqueous solution (14-18).

In this study we evaluated with a prospective, randomized clinical trial the efficacy of a chloramphenicol 0.25%–betamethasone 0.13% preparation in a gelified polyethyleneglycol 300-polyvinyl alcohol carrier, administered three times a day, when compared to a tobramycin 3%–dexamethasone 1% in aqueous solution administered four times a day. Efficacy, frequency of complications, and patient satisfaction were studied.

MATERIALS AND METHODS

Study design

This was a prospective multicentric study conducted from April to December 2004 in eight sites in Italy (academic centers and clinical practices; see Appendix). Eyes were randomized in a 1:1 ratio to receive a combination chloramphenicol 0.25%–betamethasone 0.13% gel three

times a day (Group 1) and the other to therapy with the combination tobramycin 3%–dexamethasone 1% eyedrops four times a day (Group 2) for 15 days.

Study procedures

In the study we included patients who required cataract surgery in both eyes for a visual acuity reduced to 0.2 logMAR or worse. Exclusion criteria were aimed at excluding possible inflammatory or anatomic conditions that could influence the postoperative response, and are shown in Table I.

All selected patients underwent complete ophthalmologic examination, including determination of best spectacle-corrected visual acuity (BSCVA) adopting the ETDRS table, anterior and posterior segment examination, intraocular pressure measurement with applanation tonometry, and endothelial cell counts. Estimated hardness of the lens was graded preoperatively from 1+ (soft) to 4+ (very hard). All patients signed a specifically designed informed consent and agreed to undergo the planned control examinations.

TABLE I - EXCLUSION CRITERIA

Diabetes mellitus
Use of systemic steroid or nonsteroidal drugs
Uveitis
Increased intraocular pressure
Previous ocular surgery or trauma
Subluxated lens
Endothelial cell counts of less than 1000 for mm^2
Pharmacologic mydriasis of less than 5 mm

TABLE II - SURGICAL PARAMETERS MONITORED IN THE STUDY

Topical anesthesia
Temporal clear cornea tunnel
Capsulorhexis
Intraocular lens type and model
Intracameral antibiotic
Drugs in the infusion bottle
Duration of surgery
Duration of ultrasounds
Type of viscoelastic
Type of phacoemulsification unit
Intracameral injection of myotic
Intraoperative complications
Postoperative topical medication (according to randomization list)

Preoperatively, all patients underwent prophylaxis with fluoroquinolone antibiotic eyedrops three times a day for the 3 days immediately preceding surgery. Patients underwent cataract surgery in both eyes with topical or peribulbar anesthesia, temporal incision, capsulorhexis, hydrodissection, phacoemulsification, irrigation/aspiration, foldable IOL insertion, and intraocular antibiotic injection. Several surgical parameters were monitored (Tab. II), and intraoperative complications reported. Eyes had to be excluded from the study in case of occurrence of the following intraoperative complications: posterior capsule break, anterior vitrectomy, iris chafe, and corneal suture.

One eye was operated at the time, the second one at least 7 days after the first one.

Postoperatively, one eye was randomly assigned to therapy with the combination chloramphenicol 0.25%– betamethasone 0.13% gel (Betagel, Farmila, Milano, Italy) three times a day (Group 1) and the other to therapy with the combination tobramycin 0.3%–dexamethasone 0.1% eyedrops (Tobradex, Alcon, Fort Worth, Texas, USA) four times a day (Group 2) for 15 days. On the evening of surgery, one carbonic anhydrase inhibitor tablet was administered per os. No other postoperative medications were used, otherwise the patient had to be excluded from the study. Postoperative controls were performed on days 1, 3, 7, and 15, with patients undergoing complete ophthalmologic examination, objective evaluation of the surgical eyes, as well as subjective evaluation of patient's impressions. Monitored postoperative parameters included UCVA, IOP, edema or hyperemia of eyelids and/or conjunctiva, conjunctival and/or ciliary vessels congestion, decreased corneal transparency, corneal edema, Descemet folds, presence and amount of Tyndall, pupil irregularity, synechiae, cortical remnants, pupil diameter, and IOL misplacement. Parameters 2 to 8 were graded from 0 to 4+. Subjective evaluation consisted of a simple questionnaire evaluating the presence and amount - graded in a scale from 1 to 10 - of postoperative pain, the sensation of ocular dryness, as well as evaluation of sensation change and type after therapy, and ease of therapy administration.

Statistical analysis

The primary outcome measures were visual acuity and patient satisfaction.

Statistical evaluation of differences between the two groups preoperatively, intraoperatively, and at all the considered control postoperative intervals, as well as of possible influence of operative factors on postoperative results, was performed with Stata 8.2 (Statcorp, Texas, USA) software, using Student *t*-test (preoperative data, severity of cataract, duration of surgery), Pearson chi square (intra- and postoperative parameters), Kruskal-Wallis (population differences), and analysis of variance tests (surgical parameters).

RESULTS

Demographic and baseline characteristics

Demographic and baseline characteristics of the 143 enrolled subjects (286 eyes) were as follows: mean age ± SD was 73.7±8.9 years, age ranged from 43 to 91 years, there were 53 males (37.06%) and 90 females (62.94%).

Subjects

Preoperative exclusion and inclusion criteria were respected in all cases. Table III reports preoperative clinical data of the study patients, divided according the two different therapy groups. Table IV reports severity of observed cataract, which was not statistically significant. Surgery was performed with topical anesthesia in 263 eyes, and with peribulbar in 21 eyes (Group 1 n=11, Group 2 n=10). In all eyes surgical technique was as described. In 94 eyes the infusion contained adrenaline (1 mL of 1:1000 adrenaline in 500 mL BSS) (Group 1 n= 23, Group 2 n=23), or adrenaline plus vancomycin (Group 1 n= 24, Group 2 n=24), and intraocular antibiotic (vancomycin 20 µg/mL) was injected in the anterior chamber at the end of surgery in 202 eyes (Group 1 n=102, Group 2 n=100). Duration of surgery, classified as less than 15 minutes, between 15 and 20 minutes, or longer than 20 minutes, was always less than 20 minutes. If duration of surgery was examined dividing the database according to first and second eye having surgery, first eyes showed a significantly longer surgical duration (p=0.01) (Tab. V). This is in accord with the usual policy in Italy to operate first on the eye with the most advanced cataract. Duration of ultrasound was 70.64±3.42 seconds in Group 1 and 68.80±3.31 in Group 2 (NS). Adopted viscoelastic included AMO Vitrax (sodium hyaluronate 3.0%, Advanced Medical Optics, Santa Aña, CA, USA), Duovisc (VisCoat and ProVisc [1.0% sodium hyaluronate, and 3.0% sodium

TABLE III - CLINICAL PREOPERATIVE DATA OF THE STUDY EYES (Mean ± SD)

	Group 1, Betagel (143 eyes)	Group 2, Tobradex (143 eyes)	p
Intraocular pressure, mmHg	15.55 ± 2.52	15.62 ± 2.83	ns
Pupil diameter, mm	7.12 ± 1.71	7.40 ± 1.09	ns
Endothelial cell counts, mean	2124.03 ± 431.76	2150.34 ± 441.71	ns
Endothelial cell counts, SD	186.92 ± 87.95	185.78 ± 90.04	ns
Uncorrected visual acuity	0.70 ± 0.49	0.73 ± 0.48	ns

TABLE IV - SEVERITY OF CATARACT

Severity of cataract	Group 1, Tobradex		Group 2, Betagel	
	Frequency	%	Frequency	%
1	3	2.11	3	2.11
2	57	40.14	68	47.89
3	74	52.11	67	47.18
4	8	5.63	4	2.82
Total	142	100	142	100
Mean severity	2.61	2.51		
p	ns			

hyaluronate plus 4.0% chondroitin sulfate, respectively], Alcon, Fort Worth, TX, USA), Healon (1.0% sodium hyaluronate, Pharmacia & Upjohn, Kalamazoo, MI, USA), Healon GV (1.4% sodium hyaluronate, Pharmacia & Upjohn), Healon Five (2.3% sodium hyaluronate, Pharmacia & Upjohn), IAL F (1.8% sodium hyaluronate, Bausch & Lomb-Fidia, Catania, Italy), Provisc (1.0% sodium hyaluronate physiological sodium chloride phosphate, Alcon), and VisCoat (3.0% sodium hyaluronate, 4.0% chondroitin sulfate, Alcon).

Adopted phaco units included Accurus (Alcon), Legacy (Alcon), Katalist (Chiron, Bausch & Lomb), Millennium (Karl Storz, Culver City, CA), Phaco Oertli (Oertli Instruments, Berneck, Switzerland), and Pulsar (Optikon Ophthalmic Equipment, Roma, Italy). In no case was intracameral injection of myotic used. Intraoperative complications are listed in Table VI. Intraoperative complications indicated as cause for exclusion from the study occurred in no case. Of the 143 patients, 142 completed the study, while in one patient postoperative controls on day 1, 3, and 7 were omitted. At the day 15 control no complication was observed, but nevertheless the patient was excluded from the study. Objective postoperative evaluation at all control intervals included the parameters reported in Table VII. Mean values of these parameters for Group 1 (Betagel) and Group 2 (Tobradex) are reported. Other evaluated ocular parameters, i.e., pupil irregularity, synechiae, cortical remnants, pupil diameter, IOL misplacement, occurred seldom and did not show any statistical difference between the two groups at any of the considered control intervals. Posterior segment parameters did not show any relevant difference between the two groups at any given postoperative interval.

Table VIII reports the results of this questionnaire, for parameters evaluated at all control intervals, and Table IX for conclusive patient evaluation at the end of the study, at day 15 postoperatively. Patients were questioned pertaining to the presence the feeling of pain or ocular dryness, as well as about a possible change of any ocular sensation after instillation. When a change was reported, they were questioned if it was pleasant or unpleasant. Statistical analysis showed that the two groups were comparable under all the considered parameters, with the exception of a more pleasant sensation reported after instillation of Betagel (p=0.04).

TABLE V - DURATION OF SURGERY, ACCORDING TO THE FIRST AND SECOND OPERATED EYE

	First eye, no. eyes (Group 1/Group 2)	**Second eye, no. eyes (Group 1/Group 2)**
Less than 15 minutes	80 (39/41)	99 (50/49)
Between 15 and 20 minutes	62 (28/34)	43 (25/18)
More than 20 minutes	0	0
Total	142	142

Safety

In no patients were allergic reactions or side effects related to the topically administered drugs observed.

DISCUSSION

Physics and physiology concepts sustain the ophthalmic use of a specifically designed gel as a carrier of pharmacologically active substances. This use of gel has already passed the experimental phase and is now a reality in everyday practice (14-18).

The rationale for a gel preparation is to prolong the per-

TABLE VI - INTRAOPERATIVE COMPLICATIONS

Complication	**Number of cases**	**Group 1**	**Group 2**	**%**
Insufficient mydriasis	11	4	7	3.85
Instrument malfunctioning with anterior chamber depth instability	4	2	2	1.40
Iris prolapse	1	1	0	0.35
Problems with intraocular lens insertion	9	5	4	3.15
Iris damage	0	0	0	0
Posterior capsule break	0	0	0	0
Vitrectomy	0	0	0	0
Tunnel suture	0	0	0	0

TABLE VII - POSTOPERATIVE PARAMETERS, GRADED FROM 1 TO 4+, GROUP 1 (Betagel) VS GROUP 2 (Tobradex), AT THE DIFFERENT FOLLOW-UP INTERVALS (Mean ± SD)

Parameter	Day 1	Day 3	Day 7	Day 15
UCVA				
Betagel	0.41±0.40	0.30±0.26	0.22±0.21	0.16±0.16
Tobradex	0.42±0.35	0.31±0.28	0.22±0.24	0.17±0.21
IOP				
Betagel	14.80±5.09	13.45±5.44	13.82±4.36	13.30±4.77
Tobradex	15.71±3.74	14.72±4.66	14.51±4.42	13.97±4.62
Edema of eyelids and/or conjunctiva				
Betagel	0.46±0.72	0.18±0.38	0.08±0.69	0.00±0.00
Tobradex	0.44±0.75	0.20±0.45	0.05±0.26	0.01±0.17
Hyperemia of eyelids and/or conjunctiva				
Betagel	0.76±0.82	0.32±0.48	0.06±0.23	0.04±0.06
Tobradex	0.77±0.90	0.40±0.64	0.13±0.39	0.06±0.03
Conjunctival and/or ciliary vessels congestion				
Betagel	0.53±0.66	0.17±0.38	0.02±0.14	0.00±0.00
Tobradex	0.58±0.68	0.18±0.42	0.03±0.17	0.00±0.00
Decreased corneal transparency				
Betagel	0.53±0.64	0.16±0.41	0.02±0.14	0.00±0.00
Tobradex	0.56±0.66	0.20±0.42	0.01±0.12	0.00±0.00
Corneal edema				
Betagel	0.57±0.70	0.26±0.47	0.05±0.25	0.01±0.08
Tobradex	0.64±0.75	0.20±0.44	0.08±0.27	0.00±0.05
Descemet folds				
Betagel	0.72±0.66	0.30±0.49	0.13±0.34	0.02±0.14
Tobradex	0.76±0.63	0.40±0.57	0.10±0.30	0.00±0.00
Tyndall				
Betagel	0.40±0.97	0.20±0.43	0.11±0.35	0.06±0.23
Tobradex	0.37±0.61	0.15±0.36	0.07±0.27	0.06±0.23

No differences were significant.
UCVA = Uncorrected visual acuity; IOP = Intraocular pressure

manence of the contained drugs on the ocular surface. Prolonged drug permanence provides greater pharmacologic effect, and allows for reduction in drug concentration and administration (14-18). Theoretically, all this should increase the patient's compliance and decrease possible side effects, such as ocular discomfort and allergic reactions, as well as increased intraocular pressure when steroids are administered.

Even if side effects related to ophthalmic ointment have been seldom reported, this vector has not encountered great favor for therapy after cataract surgery among ophthalmologists and patients. Ophthalmic ointments preparations are very often based on liquid paraffin, induce fogging as well as fluctuating vision, and are difficult to administer in proper and standardized amounts, especially if the vector is dense or very cold. This could lead to anterior segment lesions if the patient has reduced dexterity or must squeeze the tube with excessive strength (19). Such a risk is especially dreadful in recently operated, sutureless post-cataract eyes, and could lead to ante-

TABLE VIII - QUESTIONNAIRE FOR SUBJECTIVE EVALUATION OF PRESENCE AND AMOUNT OF POSTOPERATIVE PAIN, SENSATION OF OCULAR DRYNESS

		Day 1		Day 3		Day 7		Day 15	
		Yes	No	Yes	No	Yes	No	Yes	No
Pain	Betagel	9.15	90.85	4.93	95.07	1.41	98.59	0.00	100.00
	Tobradex	12.68	87.32	4.23	95.77	2.11	97.89	0.00	100.00
Pain	Betagel	0.30±1.05		0.08±0.40		0.02±0.19		0.00±0.00	
grading	Tobradex	0.39±1.20		0.08±0.40		0.02±0.14		0.00±0.00	
Dry eye	Betagel	22.54	77.46	31.69	68.31	24.65	75.35	16.90	83.10
	Tobradex	28.87	71.13	28.87	71.13	24.65	75.35	22.54	77.46

Values are percentages. No differences were significant

TABLE IX - QUESTIONNAIRE FOR SUBJECTIVE EVALUATION OF THERAPY AND PERSONAL COMMENTS, DAY 15 POST-OPERATIVELY

Question		Yes	No	Not reported
Did the eye sensation change after instillation of therapy?	Betagel	40.85	51.41	7.74
	Tobradex	34.51	58.45	7.04
		NS		
How was the eye sensation changed immediately after instillation of therapy?		**Not reported**	**Unpleasant**	**Pleasant**
	Betagel	23.24	2.11	74.65
	Tobradex	27.46	7.75	64.79
		p=0.04		
Was therapy easy to assume?		**Yes**	**No**	
	Betagel	100.00	0.00	
	Tobradex	98.59	1.41	
		NS		
Was it difficult to use the:	Gel (Betagel)	6.34	93.66	
	Eyedrops (Tobradex)	1.41	97.89	
		NS		

Values are percentages

rior chamber collapse.

The present study confirms that a reduced number of administrations–three instead of four–provided identical clinical results when compared to eyedrops in aqueous solution, and that the gel preparation was more pleasant for the patient than the eyedrops.

A clear limitation of this study is the number of eyes evaluated. The study was designed to demonstrate differences in postoperative pain based on the assumption that the 0–10 pain scale would have been sensible enough and that the reported postoperative pain would have been greater than what was actually observed. The majority of patients reported little or no pain, always inferior to grade 2. Only in 32 eyes was pain of grade 1 or 2 reported, which confirms the low invasiveness of modern cataract surgery. Furthermore, with such a small sample it is not possible to make any statement pertaining to endophthalmitis prevention, due to the rarity of this complication.

Severity of observed cataract was not statistically significant between the two groups. Statistical analysis showed

that the two groups were comparable under all the parameters pertaining to postoperative inflammation, despite the more frequent occurrence of grade 3–4 cataract in the Tobradex group.

Another limitation of the study is the lack of evaluation of possible viscoelastic effect on the outcome, due to the technical impossibility to impose the same viscoelastic to the involved centers.

The use of povidone-iodine in the preparation of the eye before surgery has been recognized as an important prophylactic regimen in several clinical and theoretical studies (20-25). In all the centers involved in these studies, the patient was prepared with disinfections of the periocular skin and conjunctival fornix with a povidone-iodine solution. Nevertheless, it must be pointed out that even if there are few doubts on the efficacy of preoperative povidone iodine in preventing endophthalmitis, it does not represent an absolute warranty against endophthalmitis, and it has no effect on infections developing in the postoperative period. Thus, even if pertaining literature is scarce, postoperative instillation of antibiotic eyedrops for 7–20 days is a generally accepted practice, because even a simple conjunctival infection, in the presence of a full-penetrating corneal wound, could lead to endophthalmitis (8, 9, 26).

Open-eye surgery induces a breakdown of the blood–ocular barrier and a moderate inflammation (2).

The Agency for Health Care Policy and Research recommends postoperative anti-inflammatory treatment, and the administration of a topical steroid for 7–15 days after cataract surgery is widely accepted among ophthalmologists in Europe as well as in the United States (9, 27).

In our study, the clinical postoperative evaluations did not highlight significant differences between the two therapeutic regimens. However, another limitation of this study is the lack of aqueous flare evaluation with highly sophisticated diagnostic tools such as the laser cell flare meter. It is possible that such an evaluation could demonstrate significant differences. Nevertheless, under the crude clinical point of view, apparently there were no differences, and thus it appears doubtful that the patients, on this regard, could effectively have more short or long-term benefits with one regimen than with the other.

The difference in drug administration rate between the two groups, three vs four, could be considered as a limitation. These are the customarily adopted dosages. Recommended dosage as specified by the manufacturing company is two to three times a day for the chloramphenicol/betamethasone gel combination, and four to five times a day for the tobramycin/dexamethasone eyedrops.

Theoretically, adopting respectively the lower and higher dosages would have increased the possibility to identify inadequacies of the chloramphenicol/betamethasone as well as side effects of tobramycin/dexamethasone combination. Nevertheless, we considered it more correct to use the customary dosages, and more interesting to compare under the clinical point of view.

Chloramphenicol is a low priced, broad-spectrum antibacterial agent with little evidence of bacterial resistance (28). Drug penetration into the cornea and anterior chamber after topical administration may also be an important consideration. Chloramphenicol shows a good penetration in the anterior chamber after topical administration, differently from tobramycin. The tobramycin and chloramphenicol spectra of activity include the bacteria most frequently involved in endophthalmitis, the normal eyelid bacterial flora (29-31). Chloramphenicol may induce medullar aplasia, but no study has yet shown whether its eyedrops preparation can produce systemic levels high enough to initiate myelotoxicity (28). Pertaining to the present-day spectra of activity, chloramphenicol is highly active against most Gram-negative and Gram-positive pathogens, Rickettsia and Mycoplasma. Enterobacteriaceae show variable resistance and Pseudomonas aeruginosa and mycobacteria are usually resistant. The spectrum of activity of chloramphenicol covers the majority of ocular pathogens. In a study of 738 patients with acute bacterial infections of the external eye, Seal et al found an overall resistance rate of only 6% to chloramphenicol, compared with 9% to tetracycline and around 20% to the aminoglycosides tested (32). Broad-spectrum aminoglycoside antibiotics feature over 20 years of real world proven broad-spectrum (Gram-positive and Gram-negative) efficacy against the common eye pathogens (US Dept. of Health and Human Services Orange Book. April 2006) (33, 34).

Tobramycin is active in vitro against 95% of strains of *S aureus* and *S epidermidis*, but should not be used alone as the primary drug against serious ocular infections with these aerobic Gram-positive cocci (35). This drug is used primarily in treating ocular infections with aerobic Gram-negative bacilli, thus not the typical flora causing endophthalmitis (35).

Betamethasone and dexamethasone have similar potency, duration of action, Na^+ retaining potency, for the same equivalent doses (36). Prolonged topical steroid therapy

may increase intraocular pressure in susceptible subjects, and 15 days may be enough to elicit this complication, even if the classical test of Armaly requires 20 days (37). No significant difference between the two groups was detected for this parameter in our study. We do not consider as a limitation to our study the consideration that, theoretically, prolonging the duration of therapy would have induced intraocular pressure increase in some eyes of both groups. This temporary increase is reversible with cessation of treatment, and the two adopted steroids in our study did not induce any significant increase in intraocular pressure.

In a similar study, van Endt et al compared the efficacy of postoperative treatment with fluorometholone-gentamicin versus dexamethasone-neomycin-polymyxin combination in 112 patients after cataract surgery with extracapsular technique (38). They observed statistically significant differences for postoperative conjunctival hyperemia, intraocular pressure, which was higher in the group of patients receiving the combination containing dexamethasone 0.1%. However, they protracted the treatment with the combinations up to 3 to 4 weeks after surgery. Conjunctival bacterial colony counts were also more favorable in the group receiving the fluorometholone-gentamycin combination.

Patient satisfaction with the two combinations was almost always comparable, with the gel being more pleasant to the patients, thus theoretically enhancing compliance. This is an interesting result, and theoretically the chloramphenicol/betamethasone gel combination, requiring three administrations, already offers a slight advantage in compliance. Similarly, postoperative visual acuity was comparable, indicating that both combinations offer good control of inflammation and fast rehabilitation.

In a recent study, Wallin et al stressed the importance of wound leak as well as of proper, frequent postoperative topical antibiotic administration, and they recommended fluoroquinolones (39).

CONCLUSIONS

The motivation for use of a gel is to prolong the permanence of associated drugs on the ocular surface, thus increasing potency and decreasing concentration of the drug and rate of administration, in order to decrease potential side effects and increase the patient's compliance. Our study demonstrated that an antibiotic/steroid combination in gel offers efficacy, tolerance, and good acceptance by the patients, comparable to those of a widely accepted antibiotic/steroid combination in aqueous media.

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