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Effectiveness and tolerance of piroxicam 0.5% and diclofenac sodium 0.1% in controlling inflammation after cataract surgery

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PURPOSE. *To compare the efficacy and tolerance of piroxicam 0.5% ophthalmic solution and diclofenac sodium 0.1% ophthalmic solution in controlling inflammation after phacoemulsification and intraocular lens (IOL) implantation.*
SETTING. *Ophthalmological Department, San Donà di Piave Hospital, Venice, Italy.*
MATERIALS AND METHODS. *Forty consecutive patients – 18 men and 22 women – between 55 and 85 years of age (mean age, 75.1 ± 7.12 years) who were scheduled for cataract extraction with phacoemulsification and IOL implantation were randomized to receive 0.5% piroxicam ophthalmic solution (piroxicam group, 20 patients) or 0.1% diclofenac sodium ophthalmic solution (diclofenac group, 20 patients) for 1 month postoperatively. Best-corrected visual acuity (BCVA) and intraocular pressure (IOP) measurements and slit-lamp biomicroscopy for the evaluation of corneal edema, Descemet membrane folds, Tyndall, and cells in the anterior chamber were carried out in all patients 1 day, 4 days, and 1 month postoperatively. Subjective symptoms after the nonsteroidal anti-inflammatory drug (NSAID) ophthalmic solution instillation were assessed using a questionnaire.*
RESULTS. *There were no significant differences between the two groups in postoperative IOP, BCVA, anterior chamber flare and cell levels, corneal edema, or Descemet membrane folds. Ocular discomfort, evaluated as burning or stinging sensation after NSAID ophthalmic solution instillation, was significantly more frequent and intense in the diclofenac-treated eyes. Two eyes in the diclofenac group had a mild transient punctate keratitis.*
CONCLUSIONS. *These results suggest that piroxicam is as effective as diclofenac sodium in preventing inflammation after cataract surgery with IOL implantation, and its better tolerance and safety can provide higher patient compliance. (Eur J Ophthalmol 2003; 13: 536-40)*

KEY WORDS. *Piroxicam, Diclofenac sodium, Phacoemulsification, Intraocular lens implantation, Postoperative inflammation*

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INTRODUCTION

In recent years, nonsteroidal anti-inflammatory drugs (NSAID) have been widely used in ophthalmology for topical treatment of several inflammatory ocular pathologies (1) and, in particular, several studies have demonstrated that different NSAID ophthalmic solutions are efficacious and safe in controlling postcataract surgery inflammation (2), representing a useful alternative to topical corticosteroids. In fact, NSAID appear as effective as steroidal

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agents in treatment of postoperative inflammation (3, 4), but they do not have the same associated adverse effects, such as intraocular pressure (IOP) increase, delay in reparative processes, and increased susceptibility to infections (5).

The class effect of NSAID consists of inhibition of the cyclo-oxygenase enzyme (6), with consequent reduction of the synthesis of prostaglandins, well-recognized mediators of the inflammatory processes (7).

A variety of ophthalmic formulations of NSAID have been introduced. Diclofenac sodium, a potent and rapidly acting NSAID obtained from phenylacetic acid, has been used systemically for many years and as a topical ophthalmic solution since 1989 (8). Piroxicam is a well-known NSAID agent widely used systemically to manage inflammation and pain. Recent studies have shown that piroxicam in ophthalmic solution may optimally penetrate into the ocular tissues and successfully control postoperative ocular inflammation (9).

The purpose of the present study was to compare the efficacy, safety, and tolerance of piroxicam 0.5% ophthalmic solution and diclofenac sodium 0.1% ophthalmic solution in controlling inflammation after cataract extraction with phacoemulsification and intraocular lens (IOL) implantation.

MATERIALS AND METHODS

This prospective, randomized, double-masked, parallel-groups study included 40 consecutive patients, 18 men and 22 women aged between 55 and 85 years (mean 75.1 ± 7.12 years), who were scheduled for cataract extraction with phacoemulsification and IOL implantation.

Exclusion criteria were previous intraocular surgery, presence of other ocular pathologies, diabetes mellitus, and systemic or topical treatment with steroids or NSAID in the 3 months before surgery. Particular care was used in the exclusion of dry eye syndromes, whose symptoms could mask an eye drop topical intolerance, by performing specific lacrimal function tests (corneal fluorescein staining, fluorescein break-up time test, and Schirmer *I* test).

After giving informed consent, the patients were randomized to receive diclofenac sodium 0.1% ophthalmic solution (diclofenac group) or piroxicam 0.5% ophthalmic solution (piroxicam group). Randomization was obtained using a table of random numbers.

All surgery was performed by the same surgeon (M.C.) between January and March 2002. The standard surgical procedure included peribulbar anesthesia performed by injection of 5 mL of a 1:1 mixture of lidocaine 2% and bupivacaine hydrochloride 0.5% (Marcaine).

After creation of a 3.2-mm–wide and 1.75- to 2.00-mm–long clear corneal incision (CCI) centered at the 120-degree semimeridian, a continuous curvilinear capsulorhexis (CCC) of 4.0 to 5.5 mm in diameter was performed and a bimanual phacoemulsification utilizing the divide and conquer or phaco-chop technique was carried out with a Phacoemulsifier Protegé (Storz Instruments). Before IOL implantation (AMO PhacoFlex SI-40NB Clariflex, Allergan), the CCI was slightly enlarged to 3.5 mm. The same viscoelastic solution (3% hyaluronic acid, AMO Vitrax, Allergan) was used in all cases. No corneal sutures were placed in any case.

Postoperatively, patients were instructed to instil tropicamide 0.5% eye drops once a day for 2 weeks after surgery, lomefloxacin eye drops four times daily for 2 weeks after surgery, and one of the two considered NSAID ophthalmic solutions (diclofenac sodium 0.1% or piroxicam 0.5%) four times daily for 2 weeks and then three times daily for the following 2 weeks.

Postoperative assessment of the controls, including best-corrected visual acuity (BCVA) assessment (Snellen chart), applanation tonometry, and slit-lamp biomicroscopy for evaluation of corneal edema, Descemet membrane folds, Tyndall, and cells in the anterior chamber, was carried out 1 day, 4 days, and 1 month after surgery by the same examiner (B.S.). Corneal edema and Descemet membrane folds were graduated using the criteria shown in Table I.

The number of anterior chamber cells and the flare entity were determined by one well-trained evaluator (B.S.) following the classification of Hogan and Kimura (10) reported in Table II. All the evaluations were made under standard conditions: dim room illumination, highest lamp voltage, aperture of 0.3 mm, 30 degrees of angle, 16x magnification.

Subjective symptoms after NSAID ophthalmic solution instillation were assessed using a questionnaire and graduated using the classification shown in Table III.

For statistical between-groups comparison, Kruskall-Wallis test, Student unpaired-data *t*-test, and Chi-square test were used. Statistical significance was set at $p<0.05$.

TABLE I - CORNEAL EDEMA AND DESCEMET MEMBRANE FOLDS CLASSIFICATION

Grade	Corneal edema	Descemet membrane folds
0	Absent	Absent
1	Mild sectorial edema	1–2 folds localized near the corneal tunnel
2	Sectorial edema	1–2 central folds
3	Diffuse edema	Several and diffuse folds
4	Strong diffuse edema	—

TABLE II - ANTERIOR CHAMBER FLARE AND CELL CLASSIFICATION (following Hogan and Kimura (10))

Grade	Tyndall	Cells
0	Absent	Absent
1	Trace of flare	1–5 for field
2	Mild flare	5–10 for field
3	Moderate flare (iris well visible)	10–20 for field
4	Strong flare (blurred iris)	20–50 for field
5	Very strong flare (dense aqueous)	> 50 for field

TABLE III - POSTOPERATIVE SUBJECTIVE SYMPTOMS (burning/stinging sensation)

Grade	Description
1	Absent
2	Mild
3	Moderate but transient
4	Severe
5	Intolerable

TABLE IV - PATIENT STATISTICS

Characteristics	Diclofenac group (20 patients)	Piroxicam group (20 patients)
Age (years), mean ± SD	74.2 ± 7.45	76.3 ± 7.23
Sex (M/F)	8/12	10/10
Eye (R/L)	7/13	9/11

No differences were significant by Kruskall-Wallis test

TABLE V - POSTOPERATIVE BEST-CORRECTED VISUAL ACUITY (mean ± SD)*

Follow-up (days)	Diclofenac group (20 eyes)	Piroxicam group (20 eyes)	Unpaired-data t-test (p)
1	0.66 ± 1.53	0.69 ± 1.44	NS (0.53)
4	0.85 ± 1.43	0.84 ± 1.18	NS (0.81)
30	0.92 ± 0.91	0.90 ± 0.94	NS (0.50)

*Decimal notation; NS = Not significant

TABLE VI - POSTOPERATIVE ANTERIOR CHAMBER FLARE SCORES (mean ± SD)

Follow-up (days)	Diclofenac group (20 eyes)	Piroxicam group (20 eyes)	Unpaired-data t-test (p)
1	2.05 ± 0.51	1.75 ± 0.55	NS (0.08)
4	1.10 ± 0.44	1.05 ± 0.51	NS (0.74)
30	—	—	—

NS = Not significant

RESULTS

No statistically significant differences in sex or age were found between the two groups (Tab. IV). No intra- or postoperative complications were observed in either group. All enrolled patients completed the follow-up, and postoperative treatment regimens were well tolerated with no evidence of relevant side effects.

Table V shows the mean postoperative visual outcomes in the two groups. The day after surgery, the average BCVA was 0.66 ± 1.53 in the diclofenac group and 0.69 ± 1.44 in the piroxicam group; the VA increased rapidly in the first days postoperatively and then more gradually, reaching 0.925 ± 0.91 and 0.905 ± 0.94, respectively, in the two groups 1 month after surgery. No significant differences were found in postoperative BCVA at any follow-up between the two groups.

Postoperative IOP values were ≤21 mm Hg in all eyes (data not shown). Mean postoperative flare and cell scores in the operated eyes are shown in Tables VI and VII. The highest values occurred on the first postoperative day, with average flare scores of 2.05 ± 0.51 and 1.75 ± 0.55 and mean cell scores of 2.3 ± 0.47 and 2.1 ± 0.64, respectively, in the diclofenac and piroxicam groups. These val-

ues declined rapidly in the first days after surgery and disappeared 1 month postoperatively in both groups. No differences were observed in postoperative flare and cell values between the two groups at all controls.

Mild corneal edema (mean score of 0.65 ± 0.74 in the diclofenac group and 0.40 ± 0.59 in the piroxicam group, unpaired data *t*-test not significant) and few Descemet membrane folds mostly localized near the corneal tunnel (mean score of 0.75 ± 0.78 in the diclofenac group and 0.45 ± 0.60 in the piroxicam group, unpaired data t-test not significant) were noticed in both groups at the first postoperative day only.

Considering the answers to the questionnaire (Tab. VIII), diclofenac treatment appeared associated with significantly more frequent and intense unpleasant symptoms after instillation, with six patients complaining of burning/stinging (grades 1-3) after the eye drop instillation in the diclofenac group, compared to only one patient (grade 1) in the piroxicam group. The difference between the two groups was statistically significant. Two patients in the diclofenac group presented a mild keratitis punctata that did not requires treatment interruption.

TABLE VII - POSTOPERATIVE ANTERIOR CHAMBER CELL SCORES (mean ± SD)

Follow-up (days)	Diclofenac group (20 eyes)	Piroxicam group (20 eyes)	Unpaired-data t-test (p)
1	2.30 ± 0.47	2.10 ± 0.64	NS (0.26)
4	1.10 ± 0.44	1.15 ± 0.48	NS (0.73)

NS = Not significant

TABLE VIII - PRESENCE OF POSTOPERATIVE BURNING/STINGING SENSATION DURING THE ENTIRE FOLLOW-UP

	Diclofenac group (20 patients)	Piroxicam group (20 patients)	Groups comparison (p)
No. of patients	7	1	<0.05 (0.048)*
Scores, mean ± SD	1.3 ± 0.97	0.05 ± 0.22	<0.05 (0.000)**

*Chi-square test

**Student unpaired-data *t*-test

DISCUSSION

Uneventful cataract surgery is usually followed by intraocular inflammation that can induce, in some cases, a variety of complications, including transient postoperative ocular hypertension, corneal edema, endothelial damage, posterior capsule opacification, and macular edema (11). In order to control such inflammation, various systemic and/or topical steroidal or nonsteroidal anti-inflammatory agents are commonly prescribed in the pre- and postoperative period.

Previous investigators have documented, by slit-lamp observation and fluorophotometry (2, 3), that many topical NSAID treatments are as effective as steroidal anti-inflammatory agents in controlling post-cataract surgery ocular inflammation (4), without the well-known steroid-associated risks of IOP enhancement and increased susceptibility to ocular infections (4, 5). NSAID were also demonstrated to reduce the incidence of angiographic (12) and clinically relevant cystoid macular edema (13).

Several reports have shown the efficacy of diclofenac sodium ophthalmic solution in the treatment of ocular postoperative inflammation (2, 8). Compared with other NSAID ophthalmic solutions, diclofenac sodium 0.1% was demonstrated to be similar to indomethacin 1.0% (14) and more effective than flurbiprofen 0.03% in reducing inflammation after cataract surgery and to have better subjective local tolerance than indomethacin 1.0% and flurbiprofen 0.03% (14). Piroxicam was more recently introduced as an ophthalmic solution, and a few studies have shown that it may optimally penetrate into the ocular tissues and successfully treat postoperative ocular inflammation (9).

The data of the present study indicate that piroxicam 0.5% ophthalmic solution has the same efficacy as diclofenac sodium 0.1% ophthalmic solution in controlling inflammation following cataract surgery and IOL implantation. The mean postoperative anterior chamber flare and cell scores and postoperative corneal edema and Descemet membrane folds were comparable after treatment with piroxicam and diclofenac sodium at all follow-ups (Results, Tab. VI and VII); furthermore, no significant differences were found between groups in mean postoperative BCVA at any control (Tab. V), indirectly indicating that the effectiveness in preventing postoperative cystoid macular edema was similar with both treatments. No increased postoperative IOP values were recorded in either group,

suggesting that NSAID ophthalmic solutions do not influence this parameter, as found by other authors (13).

Considering side effects, in our experience piroxicam 0.5% ophthalmic solution was associated with higher local tolerance than diclofenac sodium 0.1%, with less ocular burning/stinging after eye drop instillation (Tab. VIII). Furthermore, two cases of mild keratitis punctata in the first days postoperatively were observed in the diclofenac group, although no treatment interruption was necessary.

In conclusion, our results suggest that piroxicam 0.5% ophthalmic solution is as effective as diclofenac sodium 0.1% ophthalmic solution in controlling inflammation after cataract surgery with phacoemulsification and IOL implantation, but its better local tolerance and safety may lead to improved patient compliance.

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