Role of Topical Nepafenac and Topical Dexamethasone in Postoperative Inflammation after Cataract Surgery: A Comparative Study.

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ABSTRACT

Background: To study the role of nonsteroidal anti-inflammatory Nepafenac 0.1% topically in comparison to topical steroid for controlling postoperative inflammation after cataract surgery. **Methods:** Prospective randomized controlled trials were given and double blind study was done. In both groups, similar baseline parameters were taken into consideration. Postoperative inflammation, intraocular pressure and visual acuity following routine small incision cataract surgery were assessed in both groups in first 21 days. Parameters were graded according to severity. **Results:** There was not much difference statistically in two groups in the treatment of any of the signs, including ciliary congestion, aqueous cells, flare, descemet's folds, visual acuity and intraocular pressure (p 0.001) however, there was apparent improvement with corticosteroids when aqueous flare was considered but with Nepafenac there was no side effect and was well tolerated. **Conclusion:** Nepafenac is equally effective as topical steroid and can safely be used in routine postoperative inflammation after uncomplicated cataract surgery.

Keywords: Nepafenac a nonsteroidal anti-inflammatory drug (NSAIDS), dexamethasone phosphate, small incision cataract surgery (SICS).

INTRODUCTION

Topical steroid has been routinely used in the treatment of postoperative anterior segment inflammation as iridocyclitis. NSAIDS have been used less frequently. Nepafenac 0.1% a potent NSAID has been used lately to treat postoperative inflammation after cataract surgery and other anterior segment surgeries.[1] It was observed to be equally effective as topical corticosteroids with least side effects such as a rise in IOP. Added advantages of NSAIDS are sustained pupillary reaction and analgesia, which are must for intraocular surgeries. Postoperative cystoids macular edema is less common with the use of topical and oral NSAIDS.[2]

Even in animals, NSAIDS have shown to block arachidonic pathways limiting fibroblast activity and in turn reduce inflammation.[2]

Topical NSAIDS are good alternative to topical corticosteroids. Commonly used NSAIDS are flurbiprofen, indomethacin, ketorolac, bromfenac and nepafenac. Nepafenac seems to be more potent and well tolerated than all these.

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A prospective double blind study of efficacy and tolerability of Nepafenac 0.1% versus dexamethasone phosphate 0.1% following SICS + IOL was done in dept. of ophthalmology Teerthankar Mahaveer Medical College and Hospital Moradabad from March 2015 to August 2015. Hospital ethics committee granted approval for study.

To study the role of nonsteroidal anti-inflammatory Nepafenac 0.1% topically in comparison to topical steroid for controlling postoperative inflammation after cataract surgery.

MATERIALS AND METHODS

60 patients with senile cataract who underwent uncomplicated SICS with PCIOL implantation by one experienced surgeon were enrolled in the study after obtaining informed consent. The criteria for inclusion were age more than 25 years and uncomplicated cataract.

Exclusion criteria: Previous intraocular surgery, ocular inflammation, pseudo exfoliation, IOP more than 24 mm Hg, IDD, diabetic retinopathy, patients who had used NSAIDS in past two weeks, patients allergic to NSAIDS, one eyed person, patients with other interoperative complications.

Patients who fit in the criteria were examined thoroughly on slit lamp, IOP measured with schiotz, visual acuity measured by snellen.

Standard SICS was done with PCIOL implantation. It consisted of scleral tunnel incision, capsulorrhexis, nucleus delivery, irrigation aspiration of cortical matter, insertion of polymethyl methacrylate IOL in capsular bag. Wound was self-sealing. Methylcellulose viscoelastic used and removed at the end of surgery. Study medication topical nepafenac 0.1% or dexamethasone phosphate 0.1% was administered in a randomized double blind fashion. Computer generated schedule was done for

randomization and patients were allotted to one of the treatment schedules. Tropicamide 1% was used for all patients for preoperative dilatation of pupil. Complete care was taken to supply the topical medications (drug and placebos) to the study patients in non-identical vials. Postoperative topical medication instilled 6 times a day was continued for 21 days after surgery. 10 patients were withdrawn from the study for the following reasons: In Nepafenac group one patient developed wound gape with iris prolapse. One had severe reaction hence had to be given oral steroids. Three were irregular in follow up. In steroid group three patients had severe anterior segment inflammation and were put on oral steroids, while two were irregular in follow up. Patients were examined on 1,3,7,14 and 21st day after surgery and they were graded on following criteria, aqueous flare, cells in anterior chamber, conjunctival congestion, corneal oedema. Severity of inflammation was graded on 4 point scale ranging from 0-3 or score of three reflecting severest inflammation.

Statistical Analysis: Following tests were used to test for statistical significance

1. Chi square test for qualitative data with yate's continuity correction for 2 by 2 contingency table
2. Baseline comparison of quantitative data between groups was made using the independent sample t-tests after confirming homogeneity of variances f-max test. Changes in scores/rating across time were assessed using a two way multivariate repeated measures analysis of variance with time of assessment as the within-subject factor and drug category as the between-subject factor.
3. Since visual acuity was rated at end point only these scores were compared using the independent sample t-test as above, at end point only.

Alfa for significance was set at $p<0.05$. All tests of hypothesis were two-tailed.

RESULTS

Fifty patients were included for final analysis of anti-inflammatory response to treatment with topical nepafenac 0.1% and dexamethasone phosphate 0.1% following SICS with IOL implantation. Nepafenac group consisted of 23 patients while corticosteroid group consisted of 27 patients.

The mean (SD) age in nepafenac group was 57.67_+9.21 years and in corticosteroid group was 56.92(9.44) years. The two groups were comparable in age (t=.28 df 48 NS)

The Nepafenac group included 10 males (43%) and 13 females (56.52%) while the corticosteroid group consisted of 8 males (29.62%) and 19 females (70.38%). Two groups were similar in gender distribution (chi-square=1.22 df=1 NS)

The IOP was comparable as baseline between the two groups (t=1.29 df=42 NS) and did not vary following treatment with either nepafenac or dexamethasone phosphate.

All patients showed good compliance to the drug though analgesia could not be documented adequately among all patients. Majority of them expressed no discomfort on instillation of either drug. No secondary infection found during the study period in the selected group. Pupillary dilatation could not be studied as tropicamide was used as mydriatic drug for preoperative dilatation as well as for therapy in postoperative phase.

There were no adverse reactions observed with topical Nepafenac, which might have necessitated withdrawal of the drug from use. All subjects were analyzed on day 3, 7, 14, and 21 after surgery for signs of flare [Table 1] and cells in anterior chamber [Table 2]. Conjunctival congestion [Table 3] and corneal edema [Table 4]. These did not show any significant difference in anti-inflammatory activity between the two topical medications used. However the time to achieve the anti-inflammatory response was significant (p=0.0001). The drug and time interaction was also not significant indicating that the rate of improvement in the two drugs did not differ statistically however in terms of response of cells in the anterior chamber to the two drugs, the trend for improvement seemed to be faster and greater in magnitude with dexamethasone phosphate compared to nepafenac. Best-corrected visual acuity [Table 5] was assessed at end point only and the result between the two groups did not differ statistically.

Table 1: Mean grading of flare in postoperative period

Postoperative day	Nepafenac	Dexamethasone
1	2.05(0.75)	2.07(0.57)
3-5	1.6(0.92)	1.51(1.03)
7-9	1.12(0.8)	0.84(0.91)
14-16	0.4(0.56)	0.45(0.56)
21	0.20(.40)	0.19(0.49)

Anterior chamber flare (fine slit): 0=absent 1=mild(barely detected) 2=moderate(iris and lens details seen) 3=severe(iris and lens not visible) Main effect for group F=0.06 df=1.48 p=0.81 NS Main effect for time: Pillai's trace=0.92 F=132.94 df=4.45 p<0.0001 Group and time: Pillai's trace=0.14 f=1.79 df=4.45 p=0.15NS

Table 2: Mean grading of cells in postoperative period

Day	Nepafenac (mean SD)	Dexamethasone (mean SD)
1	2.20(0.40)	2.13(0.36)
3-5	1.40(1.01)	1.22(0.90)
7-9	1.02(0.99)	1.10(0.90)
14-16	0.85(0.83)	0.67(0.77)
21	0.65(0.75)	0.37(0.76)

Anterior chamber cells 0=none 1=1.5cells 2=6-15cells 3=15-30cells 4=30cells Main effect for group F=0.39 df=1,48, p=.53NS Main effect for time: Pillai's trace=0.90, F=102.26

df=4,45 p<0.0001 Group & time: Pillai's trace=0.18 F=2.54,df=4,45 p=0.053NS

Table 3: Mean grading of postop conjunctival congestion

Day	Nepafenac (mean SD)	Dexamethasone (mean SD)
1	1.15(0.69)	1.30(0.61)
3-5	0.82(0.75)	1.07(0.73)
7-9	0.62(0.57)	0.87(0.81)
14-	0.32(0.47)	0.37(0.69)
21	0.00(0.00)	0.11(0.32)

Conjunctival congestion: 0=none, 1=mild (some vessel injected) 2=moderate (diffuse injection) 3=severe (intense injection) Main effect of group: F=1.28, df=1.48 p=0.26 NS Main effect for time= Pillai's trace=0.79, F=42.93 Group and time: Pillai's trace=0.79 F=0.62 df=4.45 p=0.65NS

Table 4: Mean grading of postoperative corneal edema

Day	Nepafenac (mean SD)	Dexamethasone (mean SD)
1	0.78(0.82)	0.76(0.76)
3-5	0.57(0.82)	0.51(0.76)
7-9	0.32(0.55)	0.26(0.44)
14-16	0.20(0.40)	0.13(0.33)
21	0.05(0.21)	0.00(0.00)

Corneal edema: 0=nil; 1=mild; 2=moderate; 3=severe Main effect for group: F=0.22, df=1,48, p=0.64, NS Main effect for time: Pillai's trace=0.52, F=11.99, df=4,45, p=0.0001 Group and time: Pillai's trace=0.01, F=0.14, df=4,45 p=0.97 NS.

Table 5: Visual acuity

Grade	Nepafenac (n=24)	Dexamethasone (n=6)
0 (6/9-6/12)	15(62.5%)	11(42.3%)
1(6/18-6/24)	5(20.5%)	8(30.8%)
2 (6/36-6/60)	3(12.5%)	6(23.1%)
3 (<6/60)	1(4.2%)	1(3.8%)
Mean SD	1.08(0.88)	0.92(0.76)

Visual acuity did not differ significantly across the two groups (F=0.70, df=47,NS)

DISCUSSION

Nepafenac is a potent nonsteroidal anti-inflammatory agent without the side effects of topical corticosteroids, which may cause a rise in intraocular pressure, or delayed wound healing. Nepafenac has been found to be effective in controlling postoperative inflammation following small incision cataract surgery and phacoemulsification. Previous semi quantitative studies have shown Nepafenac to be an effective anti-inflammatory agent.[3-5]

Slit lamp has been used in this study for evaluation. The primary criteria to indicate reduction of anti-inflammatory response was reduction in flare and cells in postoperative phase of 21 days based on all parameters in this study including aqueous flare and cells in anterior chamber, conjunctival congestion, corneal edema, IOP, and final visual acuity.[4,5] Patients in both groups showed comparable improvement. Patients in corticosteroid group however showed marginal trend for faster and greater magnitude of improvement with greater reduction in anterior chamber cells. This suggests that there could be a role for corticosteroids in patients with severe iridocyclitis in postoperative period.

All published studies were conducted on Caucasians while our study has been done on Indian patients with brown iris. This study also shows that topical steroids need not be routinely used specially in uncomplicated surgeries. This may avoid secondary infection especially viral and rise in IOP in occasional patients who are prone. There were no adverse reactions observed in any patient with nepafenac during study period.

CONCLUSION

To conclude NSAIDS are now accepted safely as postoperative treatment modality because of their anti-inflammatory properties and analgesia as well. Nepafenac is equally effective as topical steroid and can safely be used in routine postoperative inflammation after uncomplicated cataract surgery.

Drawback of this study is that the trial has been conducted in uncomplicated patients. IOP was measured by schiotz tonometer instead of more ideal applanation tonometer. As this is a pilot study on a limited number of patients, conclusion must be drawn by a larger study.

REFERENCES

1. Gamache DA, Graff G, Brady MT. Nepafenac a unique nonsteroidalprodrug with potential utility in the treatment of trauma induced ocular inflammation: I. Assessment of anti-inflammatory efficacy. Inflammation. 2000:24:357-70.
2. Stewart WC. Preoperative and postoperative clinical evaluation of Nepafenac 0.1% ophthalmic suspension for post cataract inflammation; presented at the 2005 ASCRS meeting; Washington DCapr 2005.
3. Lane SS, Modi SS, Lehman RP. Nepafenac ophthalmic suspension 0.1% for prevention & treatment of ocular inflammation associated with cataract surgery. J. Cataract Refractive Surgery. 2007;33:53-8.
4. Miyake K, Ota I, Miyake G, Numaga J. Nepafenac 0.1% versus steroid 0.1% for preventing cystoids macular edema after cataract surgery. J. Cataract Refractive Surgery. 2011;37:1581-88.
5. Lira RP, Fulco EA, Chaves A, Dacosta PF, Arieta FR, Lira CE. Effect of Postoperative use of topical steroid and Nepafenac. Ind J Ophth. 201260(4)277-281.

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