ORIGINAL ARTICLE

To Compare the Effect of Nepafenac versus Prednisolone on Post-Operative Inflammation and Intraocular Pressure after Cataract Surgery

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ABSTRACT

Objective: To compare the effect of topical 0.1% Nepafenac and 1% prednisolone in control of inflammation and maintenance of Intraocular Pressure (IOP) after cataract surgery.

Study Design: Randomized control trial.

Place and Duration of Study: Department of Ophthalmology, from 4th June 2018 to 30th June 2019.

Materials and Methods: Total sample size of study population was 400, including all patients getting phacoemulsification cataract surgery. Study population was equally divided in two groups. Group 1 was Nepafenac group, and Group 2 was Prednisolone group. Both groups underwent cataract extraction, and were started on topical 0.1% Nepafenac or 1% Prednisolone along with topical antibiotics after surgery. Post-operative IOP and activity and flare was checked in all patients on day 1, 7 and 28 after surgery and compared between both groups.

Results: The study population had a mean age of 60.97±4.91 years. The proportion of male and female patients in study population was 51% and 49% respectively. Difference in mean post-operative IOP and mean change from pre-operative value between both groups was statistically significant (p=0.003 and 0.004 respectively). There was statistically significant difference between both groups in terms of anterior chamber cells and flare respectively at 1st week post-operatively (p=0.002, and 0.003). However, there was no statistically significant difference between both groups in terms of anterior chamber cells and flare respectively after 28 days post-operatively (p=0.12, and 0.71).

Conclusion: Nepafenac is superior to prednisolone in controlling IOP after cataract surgery, with adequate and comparable control of post-surgical inflammation.

Key Words: *Intraocular Pressure, Nepafenac, Prednisolone.*

Introduction

Cataract surgery is the most commonly performed surgery all over the world in ophthalmic eye care.[1] However like any other surgical procedure; it is also associated with a number of complications. Commonly observed post-operative complications are inflammation, infection and refractive errors.[2] Post-operative inflammation after cataract surgery remains a grave concern. This manifests as cells in Anterior Chamber (AC), proteins (flare), corneal edema and iritis.[3] This is responsible for sufficient stress to patient as well as surgeon, as post-operative surgical outcome remain compromised till settling of inflammation, which usually requires a long term management with topical and local or systemic drugs. Inflammation is managed by variety of therapeutic agents like drugs corticosteroids and other anti-inflammatory drugs. Corticosteroids are commonly used agents, which manage inflammation very well with reasonable safety. Post-operative inflammation is managed by prescription of topical corticosteroids or local steroid injections, former being commonly practiced. The drugs are safely discontinued, upon return of eye to inflammation-free state, manifested by variety of clinical signs.[4] Different corticosteroids are commonly used to treat post-cataract surgery inflammation, with different

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safety and therapeutic profiles.[5]

Conventionally, topical dexamethasone, prednisolone, loteprednol etabonate and flouromethalone are given to control inflammation after cataract surgery. A commonly observed side effect of these agents is raised Intra Ocular Pressure (IOP). Although a number of factors can result in raised IOP after cataract surgery, but in un-eventful and complication free surgery with restoration of visual acuity within days, steroids can result in raised IOP. Increased IOP can result in compression of the optic nerve leading to progressive irreversible neuropathy.

Researches are being carried out internationally to recommend a safe compound which can provide anti-inflammatory effects but with no side effects as compared to traditional steroids. Non-Steroidal Anti Inflammatory Drugs (NSAID) is widely prescribed to manage post-operative inflammation and also to provide analgesia after phacoemulsification cataract surgery. They are also shown to be beneficial in control of IOP while managing inflammation. The role of NSAIDS is also well established in prevention of post pseudophakic surgery macular oedema.[6,7]

Therefore we tried to conduct a study on comparison of efficacy and safety of Nepafenac and Prednisolone after cataract surgery. The aim of the study was to compare the effect of topical 0.1% Nepafenac and 1% prednisolone in control of inflammation and maintenance of Intraocular Pressure (IOP) after cataract surgery.

Materials and Methods

This randomized control trial was carried out after permission from hospital ethical review board in the Department of Ophthalmology, from 04 June 2018 to 30 June 2019. Written informed consent was mandatory from all patients prior to inclusion in the study. Approval from hospital's ethical review committee and written informed consent was taken from all participants. The sample size was calculated keeping level of significance as 5%, and power of the test as 80%, using World Health Organization calculator. For ease of analysis, a total sample size of 400, with 200 patients in each group was strength of study. Non-probability consecutive sampling technique was used, and all patients divided in Group 1 or 2 using lottery method. Patients with visually significant cataract undergoing cataract surgery, aged between 40-60 years from either gender were included. Patients with pre-existing glaucoma or uveitis, complicated cataract, prolonged surgery, increased phaco time, per and post-operative complications, systemic diseases e.g., diabetes, hypertension, asthma, arthritis, were excluded. All patients underwent thorough eye examination and IOP measurement was by the single researcher to exclude bias. All the patients underwent a slit lamp examination of anterior segment and assessment of IOP using applanation tonometer. All patients underwent radical and conventional phacoemulsification surgery, and all were implanted with posterior chamber intraocular lens after surgery by a single surgeon. Both groups were prescribed with 0.5% topical Moxifloxacin eye drops, three times daily for 2 weeks. Group 1 was co-started with topical 0.1% Nepafenac eye drops, thrice daily for four weeks after cataract surgery. Group 2 was started with topical 1% Prednisolone eye drops thrice daily after cataract surgery for four weeks. IOP, AC cells and flare were checked on day 1, 7 and 28 after surgery. The data collected was entered in pre-devised proforma. The data was entered and analyzed using SPSS software version 20.0. The mean and standard deviations were used to evaluate ordinal data while frequencies and percentages were calculated for nominal data variables. Normality of data was checked. Post stratification, independent't' test was used to compare mean IOP and mean change in IOP between both groups. IOP of <19mmHg after cataract surgery was considered efficacy of topical drug to control IOP. Chi square test was used to compare grading of cells and flare between both groups. p value of ≤ 0.05 was taken as statistically significant.

Results

In this study a total of 400 cases meeting the inclusion criteria were evaluated and analyzed. The groups had equal number of participants (200 each). Group 1 was Nepafenac group, in which patients were given Nepafenac and Group 2 was Prednisolone group. The clinical data of study population is given in Table (I) The comparison between both groups in terms of age, gender and laterality of eyes was statistically unremarkable. Mean pre-operative IOP and post-operative IOP along with mean change in IOP in both groups is

given in Table(I) Difference between both groups in terms of post-operative IOP and mean change in IOP was statistically significant (p=0.003 and 0.004 respectively). A higher number of patients (102/200) showed IOP control efficacy (IOP<19mmHg) in group 1 as compared to group 2 (88/200). However, the difference was not statistically significant (p=0.182). The comparison of AC cells and Flare between both groups at 1 week and 28 days is given in Table (III) The difference in AC flare and cells grading between both groups at 1 week was statistically significantly different (p=0.023 and 0.002 respectively). However, the difference in flare and cells grading at 28 days (4 weeks) after surgery was not statistically significant (p=0.216 and 0.137 respectively).

Table I: Demography and Clinical Data of Study Population (n=400)

Variable		Group 1 Loteprednol etabonate Group (n=200)	Group 2 Dexamethasone Group (n=200)	p Value Groups)
Age (Years) Mean±SD	60.97±4.91	61.3±4.89	60.63±4.99	0.603**
Gender (Male/Female)	204 /196 (51%)/ (49%)	103 /97 (51.5%)/ (48.5%)	101 /99 (50.5%)/ (49.5%)	0.297*
Laterality of eye (Right/left)	198/202 (49.5%)/(50.5%)	98/102 (49%)/ (51%)	100/100 (50%)/ (50%)	0.762*

Table II: Comparison of Pre and Post-Operative IOP

Variable	Group 1 Nepafenac Group (n=200)	Group 2 Prednisolone Group (n=200)	p Value
Mean pre - operative IOP (mmHg) Mean±SD	18.17±2.11	18.18±2.17	0.438*
Mean post - operative IOP (mmHg) Mean±SD	19.04±1.86	21.31±2.07	0.003*
Mean change in IOP (mmHg) Mean±SD	1.23±0.18	2.79±1.19	0.004*
Frequency of IOP–Pre-Operative			
12-15mmHg	22(12.2%)	17 (9.4%)	0.713**
16-19 mmHg	94(51.9%)	93 (51.4%)	
20-23 mmHg	65(35.9%)	71 (39.2%)	
Frequency of IOP –Post-Operative			
12-15mmHg	4(2%)	10 (5%)	0.182**
16-19 mmHg	98(49%)	78(39%)	
20-23 mmHg	96(48%)	104(52%)	
24 27mmHg	2(1%)	8(4%)	

Table III: Comparison of Post-Operative AC Cells and Flare between Group (n=400)

Variable	Group 1 Nepafenac Group (n=200)	Group 2 Prednisolone Group (n=200)	p Value
AC Flare – 1 week			
Grade 0	76(382%)	162 (81%)	0.023*
Grade 1	88(44%)	22 (11%)	
Grade 2	36(18%)	16 (8%)	
AC Flare – 28 days			
Grade 0	164(82%)	192(91%)	0.216*
Grade 1	36(18%)	8 (4%)	
AC Cells – 1 week			
Grade 0	86(43%)	120 (60%)	0.002*
Grade 1	62(31%)	36 (18%)	
Grade 2	42(21%)	30 (15%)	
Grade 3	10(5%)	14(7%)	
AC Cells – 28 days			
Grade 0	166(83%)	186 (93%)	0.137*
Grade 1	32(16%)	14 (7%)	
Grade 2	2(1%)	-	

Discussion

The corticosteroids are widely used after cataract surgery to control post-operative inflammation, but rise in IOP is a known complication of their use. Injudicious and prolonged use, especially in already compromised individuals puts optic nerve at risk of damage. This has been managed by limited use or use of alternative therapeutic agents.[8] We observed a mean rise of 1.23±0.18 mmHg in IOP in patients receiving Nepafenac eye drops, while a mean rise of 2.79±1.19 mmHg was observed in Prednisolone group. In a study conducted for evaluation of IOP rise after Prednisolone use after cataract surgery, it was observed that 3% of patients has high IOP after cataract surgery.[9] Since the difference in change in IOP was significant between groups, we recommend use of Nepafenac in patients particularly susceptible to glaucomatous damage. There have been multiple researches evaluating safety, performance and analysis of NSAIDS after phacoemulsification

surgery. In a study evaluating post-operative inflammation by laser photometry, it was observed that Nepafenac was superior to other NSAIDs in controlling post-operative inflammation.[10] We used topical Nepafenac in concentration of 0.1%, given thrice daily for four weeks. Some studies evaluated the dose of Nepafenac, and found out that 0.1% Nepafenac was equally effective to 0.3% Nepafenac with less adverse effects.[11] In another study comparing efficacy of Nepafenac with placebo drug, it was observed that Nepafenac was far superior in managing post-surgical inflammation.[12] In the most reliable meta-analysis evaluating 19 controlled trials, it was observed that Nepafenac was superior to all NSAIDs in managing post-operative pain, while management of AC inflammation after cataract surgery was superior by Diclofenac followed by nepafenac eye drops.[13]

There have been some studies mentioning the superiority of steroids in maintaining mydriasis during cataract surgery if used before surgery. However some studies have shown equal efficacy of Nepafenac and Prednisolone in maintaining mydriasis during phacoemulsification.[14] This is to prove non-inferiority of NSAIDs to steroids in managing per-operative mydriasis.

In another study conducted for comparison of Nepafenac and Prednisolone in controlling inflammation after small gauge vitrectomy, it was observed that Nepafenac was superior to Prednisolone in managing post-operative pain, and was equal in efficacy in management of post-operative inflammation.[15] In other studies comparing safety profile of NSAIDs and steroids in management of inflammation after cataract surgery, it was observed that Diclofenac was equal to Prednisolone in management of inflammation, and was equally safe and well-tolerated.[16] Similar findings were observed by Malik A and colleagues, who observed that NSAIDS like nepafenac, bromfenac and ketorolac are a good alternative to steroids in management post-operative ocular inflammation.[17]

We observed that there was statistically significant difference in grading of AC cells and flare between both groups at 1 week after surgery. However, the difference was not statistically significant at 4 weeks after surgery. This is in connection with results found out by Simone JN et al who found out that Prednisolone was superior to Nepafenac in management of ocular inflammation at 1 week, which was comparable at one month after surgery.[18] We used either Nepafenac or Prednisolone along with antibiotic after surgery. In another study, it was revealed that Diclofenac alone, or used in combination with Dexamethasone was superior to Dexamethasone alone in prevention of development of pseudophakic macular edema, and change in central retinal thickness.[19]

There have been conflicting results with regards to superiority of NSAIDs in post-operative pain and inflammation. In one meta-analysis, gross results showed the superiority of NSAIDS in management of post-operative inflammation as compared to corticosteroids. However, the results also showed the better results of NSAIDS in prevention of Irvine Gass syndrome (pseudophakic cystoid macular oedema).[20] In one meta-analysis evaluating 48 randomized control trials, no conclusion was found regarding superiority of NSAIDs to steroids in management of post-operative inflammation or pain.[21]

Our study has limitation of not having a group using combination of NSAIDS and steroids for management of inflammation and evaluation of IOP. The management of post-operative pain using visual analogue score could also have been beneficial. The follow up time of 4 weeks after surgery was also slightly shorter, considering that inflammation might continue for 6 to 8 weeks after surgery.

Conclusion

We conclude that Nepafenac was safer in control of IOP after phacoemulsification cataract extraction surgery. The control of post-operative inflammation is better with use of steroids immediately after cataract surgery. However, in long term, both drugs show equal efficacy in management of post-operative inflammation. Nepafenac is thus a safe and efficient alternative to Prednisolone in patients undergoing un-eventful cataract surgery.

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