Effect of Post-cataract Surgery Topical NSAID Plus Steroid Vs Topical Steroid Alone on Central Macular Thickness

Bhushan Vishwas Chaudhari^{1*}, Madhav J Bhat², Aartee Palsule³

¹MBBS, D.O., DOMS, DNB, FICO (UK), Assistant Professor, Department of Ophthalmology, T N Medical College And B Y L Nair Charitable Hospital, Mumbai, Maharashtra, India; ^{2,3}Consultant, Department of Ophthalmology, Deenanath Mangeshkar Hospital and Research Centre, Pune, Maharashtra, India.

ABSTRACT

Introduction: An uneventful cataract surgery can lead to retinal changes including subclinical cystoid macular oedema. The use of NSAID preoperatively and steroids and NSAID combination postoperatively reduces the incidence of pseudophakic cystoid macular oedema.

Objective: To compare the effect of post-cataract surgery topical NSAID (bromfenac 0.09%) plus steroid (prednisolone acetate 1%) use to that of topical steroid (prednisolone acetate 1%) use alone on central macular thickness assessed by Optical Coherence Tomography (OCT).

Methods: A prospective, observational, comparative study including 100 eyes of 100 patients who underwent uncomplicated Small Incision Cataract Surgery with PCIOL implantation. Among these, 50 operated eyes of 50 patients were started postoperatively on topical bromfenac 0.09% with prednisolone acetate 1% (Group 1) and 50 operated eyes of other 50 patients were started postoperatively on topical Prednisolone acetate 1% alone (Group 2). The patients were randomly distributed into two groups. The Subfoveal thickness, Parafoveal thickness and Perifoveal thickness of macula on OCT of both groups were noted preoperatively a day before surgery and postoperatively at Day1, 2weeks and 4weeks.

Results: The study included sixty males and forty females.33.0% patients belonged to 50-59 years, 42.0% to 60-69 years and 25.0% to 70-79 years. There was a statistically significant increase in mean Subfoveal thickness, mean Parafoveal thickness and mean Perifoveal thickness in Group 2 patients as compared to Group 1 patients postoperatively at 2 weeks and 4 weeks.

Conclusion: The central macular thickness in the early postoperative period is significantly less in patients on postoperative topical NSAID and steroid as compared to those on postoperative topical steroid alone. Adding a topical NSAID to a topical steroid postoperatively has a beneficial effect on Central macular thickness.

Key Words: Bromfenac 0.09%, Prednisolone acetate 1%, Small Incision Cataract Surgery, Optical Coherence Tomography, Central macular thickness

INTRODUCTION

Cataract surgery is one of the most common and most effective surgical procedures performed worldwide.¹ However, uneventful cataract surgery can lead to minor retinal changes including subclinical cystoid macular oedema and angiographically detected retinal leakage. The use of optical coherence tomography (OCT) in the postoperative period enables the detection of subclinical changes in macular thickness.²⁻⁵

The main mechanism involved in macular oedema is considered to be inflammation. In general, intraocular surgery

seems to trigger the accumulation of macrophages and neutrophils that are further activated by circulating inflammatory agents, including cyclooxygenase and lipoxygenase metabolites, proteolytic agents and more, leading to the appearance of clinical signs of inflammation.⁶Arachidonic acid is metabolized by cyclooxygenase to prostaglandins which are the most important lipid-derived mediators of inflammation.⁷Phospholipids in the cell membrane are the substrate for phospholipase A2 to generate arachidonic acid from which prostaglandins and leukotrienes are produced.⁸Surgical trauma triggers arachidonic acid cascade which in turn generates prostaglandins by activation of

Corresponding Author:

Bhushan Vishwas Chaudhari, Department of Ophthalmology, T N Medical College And B Y L Nair Charitable Hospital, Mumbai, Maharashtra, India; Email: bhushan.chaudhari86@gmail.com

ISSN: 2231-2196 (Print)

ISSN: 0975-5241 (Online)

Received: 16.05.2021

Revised: 12.07.2021

Accepted: 03.10.2021

Published: 13.12.2021

COX-1 and COX-2.⁸ Non-steroidal anti-inflammatory drugs (NSAIDs) inhibit the enzyme cyclooxygenase which is required for the production of prostaglandins.⁹ Corticosteroids interfere with the activity of Phospholipase A2, thereby inhibiting the release of arachidonic acid and the production of all arachidonic acid metabolites, including prostaglandins.¹⁰ The prophylactic use of non-steroidal anti-inflammatory drugs preoperatively and the combination of steroids and non-steroidal anti-inflammatory drugs in the postoperative period is recommended to reduce the incidence of pseudophakic cystoid macular oedema.¹¹

Optical Coherence Tomography is a relatively new method for high-resolution cross-sectional imaging of the retina that directly measures changes in the z-plane (depth of retina).¹² It is possible to obtain noncontact, high resolution, cross-sectional imaging of the retina. This ability of OCT to image tissue morphology in situ and real-time has been termed "optical biopsy".¹³

In our study, we compared the effect of topical NSAID (bromfenac 0.09%) plus steroid (prednisolone acetate 1%) use to that of topical steroid (prednisolone acetate 1%) use alone after cataract surgery on central macular thickness, which was assessed by Optical Coherence Tomography.

MATERIALS AND METHODS

This prospective, non-interventional, observational, comparative study included 100 eyes of 100 patients who underwent uncomplicated Small Incision Cataract Surgery (SICS) with 'in the bag' rigid Polymethyl methacrylate (PMMA) Posterior Chamber Intraocular Lens (PCIOL) implantation. Among these, 50 operated eyes of 50 patients were started postoperatively on topical bromfenac 0.09% twice a day along with prednisolone acetate 1% four times a day both for four weeks (Group 1) and the 50 operated eyes of other 50 patients were started on topical prednisolone acetate 1% alone four times a day for four weeks (Group 2). Topical prednisolone acetate 1% was tapered gradually after 4 weeks in both the groups.

The study was approved by the Institutional Ethics Committee (DCGI Reg No ECR/15/Inst/ Maha/2013) of Deenanath Mangeshkar Hospital and Research Centre, Pune. Inclusion criteria were patients with normal preoperative central macular thickness who underwent Small incision cataract surgery (SICS) with 'in the bag' rigid PMMA PCIOL implantation. Patients who were ready to participate in the study and gave informed consent were included. Signal strength 5 or more on optical coherence tomography was an inclusion criterion. Single surgeons performed all the surgeries using the same technique. The patients with ocular surface disorders, central corneal opacities, glaucoma, uveitis, dense cataract, posterior segment pathology and other ocular pathologies affecting the macula, etc were excluded. Also, patients with systemic

diseases like diabetes, hypertension, ischemic heart disease, etc were excluded. Patients undergoing complicated SICS and who had previous intraocular surgeries, patients with inferior quality measurement of Optical coherence tomography were excluded.

There were two groups with a random distribution of patients. Group 1 with patients on postoperative topical NSAID bromfenac 0.09% twice daily and topical steroid prednisolone acetate 1% four times daily both for four weeks and Group 2 included patients started postoperatively on topical steroid prednisolone acetate 1% alone four times a day for four weeks.

Patient history including present ocular complaints, use of any topical medications, history of any ocular disease or intraocular surgeries was noted. History of systemic illnesses including diabetes, hypertension, ischemic heart disease, etc was noted. Detailed Ocular examination of all patients was done, which included distant and near visual acuity, slit-lamp examination, applanation tonometry, dilated fundus examination with indirect ophthalmoscopy, keratometry, biometry with intraocular lens power calculation and optical coherence tomography after pupillary dilatation. Optical Coherence Tomography was done using the Carl Zeiss Cirrus HD spectral-domain OCT machine using macular cube 512 × 128 as shown in Figures 6 and 7.

All patients were examined on the same OCT machine by the same examiner.

The central macula was divided into 9 areas: Subfoveal thickness (SFT = F1) included a central macular area of 1 millimetre in diameter, the Parafoveal thickness (ParaFT) (F2-F5) included 4 quadrants and measured 2.22 millimetres in diameter and the perifoveal thickness (PeriFT) (F6-F9) included 4 quadrants and measured 3.45 millimetres in diameter. Regional variables parafoveal thickness = $(F2 + F3 + F4 + F5)/4$ and perifoveal thickness = $(F6 + F7 + F8 + F9)/4$. OCT was done at baseline a day before cataract surgery and postoperatively at day 1, 2 weeks and 4 weeks.

Surgical procedure: SICS with 'in the bag' rigid non-foldable PMMA PCIOL implantation was performed by the same surgeon using the same technique in all the patients. Postoperatively all the patients were started on an oral antibiotic, oral NSAID and oral Proton pump inhibitor for 5 days and also on the same topical antibiotic eye drops and prednisolone acetate 1% eye drops four times a day for four weeks initially and then tapered over a month in the operated eye. Patients were followed up on Day 1, at 2 weeks and 4 weeks postoperatively.

STATISTICAL METHODS

Statistical analysis is carried out using SPSS (version 20) for the windows package (SPSS Science, Chicago, IL, USA).

The description of the data is done in form of Mean $\pm$ SD for quantitative data. The unpaired t-test is used to test the statistical significance of difference of macular thickness measurements at every point between the two groups. A P-value of <0.05 is considered significant.

RESULTS

Sixty males and forty females were enrolled in the study as shown in Figure 1. 33.0% patients belonged to the age group 50-59 years, 42.0% patients belonged to 60-69 years and 25.0% patients belonged to 70-79 years as represented in Figure 2.

The study involved patients with nuclear sclerosis grade II, Nuclear sclerosis grade III and Posterior Subcapsular cataracts. The grade of cataracts was comparable in the groups. The mean Subfoveal thickness, mean Parafoveal thickness and mean Perifoveal thickness of macula on OCT of both the Groups were noted a day before surgery and postoperatively at Day 1, 2 weeks and 4 weeks. There was no statistically significant difference in preoperative mean Subfoveal thickness, mean Parafoveal thickness and mean Perifoveal thickness of macula between the two groups. The mean Subfoveal thickness, mean Parafoveal thickness and mean Perifoveal thickness in Group 1 and Group 2 patients postoperatively at 2 weeks was $253.77 \pm 15.50 \mu\text{m}$, $319.08 \pm 23.48 \mu\text{m}$, $273.20 \pm 22.23 \mu\text{m}$ and $266.95 \pm 16.47 \mu\text{m}$, $338.90 \pm 23.89 \mu\text{m}$, $305.93 \pm 73.67 \mu\text{m}$ respectively and at 4 weeks was $241.97 \pm 14.14 \mu\text{m}$, $304.13 \pm 22.75 \mu\text{m}$, $261.20 \pm 20.69 \mu\text{m}$ and $250.15 \pm 14.68 \mu\text{m}$, $322.60 \pm 23.38 \mu\text{m}$, $284.43 \pm 60.47 \mu\text{m}$ respectively as depicted in Tables 1, 2 and 3 and Figures 3, 4 and 5.

There was a statistically significant increase in mean Subfoveal thickness, mean Parafoveal thickness and mean Perifoveal thickness in Group 2 patients as compared to Group 1 patients postoperatively at 2 weeks and 4 weeks.

DISCUSSION

This prospective observational non-interventional study was conducted to assess the effect of post-cataract surgery topical medications on the central macular thickness. The central macular thickness was measured by Optical Coherence Tomography.

In our study, there was a significant increase in central macular thickness at 2 weeks and 4 weeks after uncomplicated Small Incision Cataract Surgery amongst those on topical prednisolone acetate 1% alone postoperatively as compared to those on postoperative topical bromfenac 0.09% and prednisolone acetate 1%. Similarly, a study by Li N et al. demonstrated that the postoperative mean foveal thickness

was significantly higher at 1 month after phacoemulsification cataract surgery among patients treated with dexamethasone only compared with those who received bromfenac plus dexamethasone.¹⁴ Also in a study done by David R.P. et al. ketorolac was used. It demonstrated a statistically significant difference in total macular volume values between the control and ketorolac treatment groups 1 month after surgery with the ketorolac group having 45.8% less macular swelling on OCT.¹⁵ Thus, suggesting that NSAID use causes less post-operative macular swelling. Wolf and colleagues conducted a similar study in which the control group (prednisolone) and the study group (prednisolone-nepafenac) were evaluated and compared concerning the presence of pseudophakic macular oedema with 4 weeks follow up. Five patients in the control group had visually significant pseudophakic macular oedema compared to zero patients in the study group.¹⁶

CONCLUSION

The central macular thickness in the early postoperative period is significantly less in patients on postoperative topical NSAID (bromfenac 0.09%) and steroid (prednisolone acetate 1%) as compared to those on postoperative topical steroid (prednisolone acetate 1%) alone.

The study demonstrated that adding a topical NSAID to a topical steroid postoperatively prevents a significant rise in Central macular thickness in the early postoperative period.

ACKNOWLEDGEMENT

The support of all staff and colleagues of the ophthalmology department of Deenanath Mangeshkar Hospital and Research Centre is gratefully acknowledged. I am thankful to all the patients who co-operated and helped us make this contribution.

We the authors of this study acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. We are also grateful to authors/editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

Conflict of Interest: NIL

Source of Funding: NIL

Author's Contribution:

The concept and Design of the study were done by Bhushan Vishwas Chaudhari, Madhav J Bhat and Aartee Palsule. Data acquisition and analysis were done by Bhushan Vishwas Chaudhari. Manuscript preparation, editing done by Bhushan Vishwas Chaudhari, Madhav J Bhat and Aartee Palsule.

REFERENCES

1. Thompson J, Lakhani N. Cataracts. Prism Care.2015 Sep;42(3):409-23
2. Growing R, Becker H. Retinal thickness immediately after cataract surgery measured by optical coherence tomography. Ophthalmic Surg Lasers. 2000 May-Jun;31(3):215-7.
3. Sourdille P, Santiago PY. Optical coherence tomography of macular thickness after cataract surgery. J Cataract Refract Surg. 1999 Feb;25(2):256-61.
4. Kim SJ, Equi R, Bressler NM. Analysis of macular oedema after cataract surgery in patients with diabetes using optical coherence tomography. Ophthalmology. 2007 May;114(5):881-9.
5. Biro Z, Balla Z, Kovacs B. Changes of the foveal and perifoveal thickness measured by OCT after phacoemulsification and IOL implantation. Eye (Lond). 2008 Jan;22(1):8-12.
6. Miltiadis KT, Chrysanthi T, Vasilios D, Aleksandra K and Ioannis P. Textbook of Cataract Surgery. Section 3 Complications. Chapter 22 Macular Edema and Cataract Surgery .2010: 323-36.
7. Ahuja M, Dhake AS, Sharma SK, Majumdar DK. Topical ocular delivery of NSAIDs. AAPS J. 2008 Jun;10(2):229-41.
8. McColgin AZ, Heier JS. Control of intraocular inflammation associated with cataract surgery. Curr Opin Ophthalmol. 2000 Feb;11(1):3-6.
9. Flach AJ. Topical nonsteroidal anti-inflammatory drugs in ophthalmology. Int Ophthalmol Clin. 2002 Winter;42(1):1-11.
10. Polansky JR, Weinreb RN. Steroids as anti-inflammatory agents. In: Sears ML, editor. Pharmacology of the Eye. New York, NY: Springer-Verlag; 1984. pp.460-538.
11. Rho DS. Treatment of acute pseudophakic cystoid macular oedema: Diclofenac versus ketorolac. J Cataract Refract Surg. 2003 Dec;29(12):2378-84.
12. Ferrari TM, Cavallo M, Durante G, Mininno L, Cardascia N. Macular edema induced by phacoemulsification. Doc Ophthalmol. 1999;97(3-4):325-7.
13. Gallagher MJ, Yilmaz T, Cervantes-Castaneda RA, Foster CS. The characteristic features of optical coherence tomography in posterior uveitis. Br J Ophthalmol. 2007 Dec;91(12):1680-5. Epub 2007 Jun 25.
14. Li N, Wang G-Q, Peng X-J, Wang J, Sui Y-L. Effects of bromfenac sodium eye drop used in the perioperative period on macular foveal thickness after cataract surgery: a primary study. Int Eye Sci. 2015;15(10):1802-4.
15. Almeida DR, Johnson D, Hollands H, Smallman D, Baxter S, Eng KT, et al. Effect of prophylactic nonsteroidal antiinflammatory drugs on cystoid macular oedema assessed using optical coherence tomography quantification of total macular volume after cataract surgery. J Cataract Refract Surg. 2008 Jan;34(1):64-9.
16. Wolf EJ, Braunstein A, Shih C, Braunstein RE. Incidence of visually significant pseudophakic macular oedema after uneventful phacoemulsification in patients treated with nepafenac. J Cataract Refract Surg. 2007 Sep;33(9):1546-9.

Figure 1: Sex wise distribution of patients.

Figure 2: Age wise distribution of patients.

Figure 3: Comparison of OCT Mean SFT between the groups on Postoperative topical NSAID plus Steroid(Group 1) and Steroid alone (Group 2).

Figure 4: Comparison of OCT Mean ParaFT between the groups on Postoperative topical NSAID plus Steroid (Group 1) and Steroid alone (Group 2).

Figure 5: Comparison of OCT Mean Peri FT between the groups on Postoperative topical NSAID plus Steroid(Group 1) and Steroid alone (Group 2).

Figure 6: Carl Zeiss Cirrus HD spectral domain optical coherence tomography (OCT) machine.

Figure 7: OCT- Macular cube 512 × 128 showing normal pre-operative central macular thickness.

Table 1: Comparisons of OCT mean Sub-foveal thickness (SFT) among those using postoperative NSAID plus steroids (Group 1) and those using postoperative Steroids alone (Group 2).

Groups	Preoperative SFT (Mean $\pm$ SD) in μm	Postoperative Day1 SFT (Mean $\pm$ SD) in μm	Postoperative 2weeks SFT (Mean $\pm$ SD) in μm	Postoperative 4weeks SFT (Mean $\pm$ SD) in μm
NSAID plus Steroid	241.17 $\pm$ 13.65	245.15 $\pm$ 13.56	253.77 $\pm$ 15.50	241.97 $\pm$ 14.14
Steroid alone	243.20 $\pm$ 12.08	250.35 $\pm$ 13.86	266.95 $\pm$ 16.47	250.15 $\pm$ 14.68
P value	0.447, Not Significant	0.06, Not Significant	0.00, Significant*	0.006, Significant*

Table 2: OCT means parafoveal thickness (Para-FT) among those using postoperative NSAID plus Steroid (Group 1) and those using postoperative Steroid alone (Group 2).

Groups	Preoperative ParaFT (Mean $\pm$ SD) in μm	Postoperative Day 1 ParaFT (Mean $\pm$ SD) in μm	Postoperative 2weeks ParaFT (Mean $\pm$ SD) in μm	Postoperative 4weeks ParaFT (Mean $\pm$ SD) in μm
NSAID plus Steroid	312.12 $\pm$ 21.96	308.4 $\pm$ 23.17	319.08 $\pm$ 23.48	304.13 $\pm$ 22.75
Steroid alone	315.53 $\pm$ 23.71	318.5 $\pm$ 22.12	338.90 $\pm$ 23.89	322.60 $\pm$ 23.38
P value	0.463, Not Significant	0.032, Significant*	0.00, Significant*	0.00, Significant*

Table 3: OCT means perifoveal thickness (Peri-FT) among those using postoperative NSAID plus Steroid (Group 1) and those using postoperative Steroid alone (Group 2).

Groups	Preoperative Peri-FT (Mean $\pm$ SD) in μm	Postoperative Day1 Peri-FT (Mean $\pm$ SD) in μm	Postoperative 2weeks Peri-FT (Mean $\pm$ SD) in μm	Postoperative 4weeks Peri-FT (Mean $\pm$ SD) in μm
NSAID + Steroid	267.22 $\pm$ 16.81	265.37 $\pm$ 18.25	273.20 $\pm$ 22.23	261.20 $\pm$ 20.69
Steroid alone	271.45 $\pm$ 14.28	276.38 $\pm$ 14.49	305.93 $\pm$ 73.67	284.43 $\pm$ 60.47
P value	0.194, Not Significant	0.002, Significant*	0.002, Significant*	0.007, Significant*