

Impact of Topical Nepafenac on Macular Thickness after Phacoemulsification with Intraocular Lens Implantation in Patients without Diabetic Retinopathy

Arooj Amjad¹, Muhammad Shaheer², Hassan Tariq³, Ammarah Rasheed⁴

¹ Assistant Professor, Post-graduate Medical Institute, Lahore.

³ Post-graduate Resident, Lahore General Hospital, Lahore.

² Assistant Professor, King Edward Medical University, Lahore.

⁴ Biostatistician, King Edward Medical University, Lahore.

Author's Contribution

¹ Conception of study

^{1,2,3} Experimentation/Study conduction

^{3,4} Analysis/Interpretation/Discussion

^{1,2} Manuscript Writing

² Critical Review

⁴ Facilitation and Material analysis

Corresponding Author

Dr. Muhammad Shaheer,

Assistant Professor,

COAVS/KEMU,

Lahore

Email: mshaheer212@gmail.com

Article Processing

Received: 10/01/2022

Accepted: 31/01/2022

Cite this Article: Amjad, A., Shaheer, M., Tariq, H., Rasheed, A. Impact of Topical Nepafenac on Macular Thickness after Phacoemulsification with Intraocular Lens Implantation in Patients without Diabetic Retinopathy. Journal of Rawalpindi Medical College. 30 Jun. 2022; 26(2): 301-305.

DOI: <https://doi.org/10.37939/jrhc.v26i2.1877>

Conflict of Interest: Nil

Funding Source: Nil

Access Online:



Abstract

Objective: To study the effect of post-operative Non-Steroidal Anti-inflammatory (NSAID) eye drops on macular thickness in patients without diabetic retinopathy measured by Optical Coherence Tomography (OCT) after cataract surgery.

Study Design: Quasi-experimental study.

Place & Duration of Study: Ophthalmology Department/Lahore General Hospital, Lahore from 15-01-2019 to 31-12-2021.

Materials & Methods: Diabetic patients without retinopathy who required cataract surgery for visual rehabilitation were included in the study. They were then divided into two groups. Group A included patients who received routine steroid+antibiotic post-operative drops while Group B comprised patients who received nepafenac (0.1%) eye drops eight hourly in addition to routine post-operative eye drops. All patients underwent standard phacoemulsification and intraocular lens implantation followed by the use of NSAID eye drops for a month. OCT measurements were done pre-operatively, 7 and 28 days post-operatively.

Results: Comparison of central macular thickness between groups was significant at (Pre & 7-day post-op) and insignificant at (7th day & 28th day post-op) and (Pre & 28th day post op) i.e. 0.043, 0.834, and 0.084 respectively. However, a difference in mean central macular thickness was significant in all follow-up periods i.e. 0.003, 0.006, and 0.000

Conclusion: Post-operative NSAID in diabetic patients without retinopathy leads to a significant decrease in macular thickness as compared to those who do not receive post-operative NSAID after cataract surgery.

Keywords: Phacoemulsification, Optical Coherence Tomography, Non-steroidal Anti-Inflammatory Agents.

Introduction

Phacoemulsification is the most commonly executed cataract surgery globally. The cause of cataracts is opacification of the crystalline lens due to any reason which is removed and substituted by an intraocular lens.¹ Phacoemulsification is the preferred choice for cataract surgery owing to its early visual rehabilitation and fewer post-operative complaints.^{2,3}

Non-steroidal anti-inflammatory drugs (NSAIDs) are being used by ophthalmologists for a long time. Food and drug administration in the United States has approved Nepafenac, ketorolac, diclofenac, flurbiprofen, and bromfenac for use. The pharmacologic characteristics of these NSAIDs vary but eventually, all of them inhibit the activation of the cyclooxygenase enzyme. This in turn halts the production of inflammatory markers resulting in reduced inflammation.^{4,5}

Nepafenac is an amide analog of the Non-steroidal anti-inflammatory drug amfenac which is mainly used for the treatment of ocular inflammation post-surgery and in various vitreoretinal disorders owing to its rapid penetration and early achievement of minimum inhibitory concentration levels.^{6,7} In addition to that NSAIDs have been used for pain relief after ophthalmic surgical procedures.⁸

Mathys KC and Cohen KL have studied the effects of topical nepafenac on the macular thickness after cataract surgery. In their study, macular thickness increased almost twice in the control group as compared to the nepafenac group. They concluded nepafenac to be safe during the post-operative period and effective in reducing the macular thickness.⁹ Tzelikis et al studied the impact of topical nepafenac 0.1% in thwarting macular edema after intraocular lens implantation. At five weeks topical nepafenac was effective in preventing macular edema as compared to controls.¹⁰ Kwon S II et al have defined macular edema as a more than 30% increase from baseline and the incidence of developing macular edema is more in diabetics than non-diabetics.¹¹ Only one local study was found in local literature that too was on patients with diabetic retinopathy.

Materials and Methods

Ethical approval of this study was obtained from the Institutional review board of Post Graduate Medical Institute, Lahore. A sample size of 40 was calculated using a 95% confidence interval and absolute precision of 0.10.¹² One hundred and ten patients were selected

by non-probability consecutive sampling that fulfilled the inclusion and exclusion criteria. Patients presenting to the Eye OPD Lahore General Hospital were assessed for inclusion and exclusion criteria. All diabetic patients without retinopathy and with cataracts requiring surgery were included in the study after informed consent. Patients diagnosed with any corneal pathology i.e. corneal opacity hindering OCT measurement and those having any coexisting ocular pathology or infection were excluded. Patients were allocated to two groups A and B (Fifty-five patients each). Group A included patients who received routine steroid+antibiotic post-operative drops while Group B comprised patients who received nepafenac (0.1%) eye drops eight hourly in addition to routine post-operative eye drops.

After aseptic measures, opsite was applied to the eye to be operated and a stab incision was made at the limbus. Viscoelastic was injected into the anterior chamber and continuous curvilinear capsulorhexis was performed. The lens nucleus is separated from the lens cortex and the lens cortex is separated from the lens capsule by hydro dissection and hydrodilatation. The lens was then emulsified by phacoemulsification and an intraocular lens implanted. Post-operative steroid and antibiotic drops were given every 4 hours for two weeks and 4 times daily for the next four weeks in tapering dosage in addition to nepafenac 0.1% eye drops thrice daily. Visual acuity and OCT for macular thickness were recorded pre-operatively and 7, 28th day post-operatively. Data Analysis was done on SPSS version 22. Quantitative variables were represented by mean and standard deviation whereas qualitative variables were presented as frequency and percentage.

Mann Whitney test was applied to check the difference between both groups. A p-value of ≤ 0.05 was considered significant.

Results

A sample of one hundred and ten patients was equally divided into two groups with almost equal distribution of male and female gender. Comparison of central macular thickness between groups was significant at (Pre & 7-day post-op) and insignificant at (7th day & 28th day post-op) and (Pre & 28th day post op) i.e. 0.043, 0.834, and 0.084 respectively. However, a difference in mean central macular thickness was significant at all follow-up periods i.e. 0.003, 0.006, and 0.000 (Table 4). Similarly, the difference between the mean macular cube at all follow-up intervals was significant i.e. 0.000, 0.049, and 0.000 (Table 5).

Table 1: Descriptive statistics

Sr. No.		Group 1			Group 2		
		Minimum	Maximum	Total	Minimum	Maximum	Total
1	Age	47	76	55	48	72	55
2	Gender	Male 28(50.9%)	Female 27(49.1%)	55	Male 27(49.1%)	Female 28(50.9%)	55
3	Operated eye	Right 27(49.1%)	Left 28(50.9%)		Right 27(49.1%)	Left 28(50.9%)	

Table 2: Visual Acuity

Sr. No.	VA	Group 1	Group 2	P value
1	Pre-operation	0.8873±0.2028	0.8582±0.1950	0.129
2	7 th Post operation	0.0782±0.1674	0.1218±0.1739	0.083
3	28 th Post-operation day	0.0182±0.05803	0.0255±0.0673	0.543

Table 3: Macular Thickness (Centre & Cube) and Signal Strength

Sr. No.	Macular thickness (Centre)	Group 1	Group 2
1	Pre-operation day	213.818±13.6049	225.1273±7.76520
2	7 th Post-operation day	219.6182±9.75912	222.5400±12.44224
3	28 th Post-operation day	215.4000±7.60507	215.2909±11.1283
	Macular thickness (Cube)	Group 1	Group 2
4	Pre-operation day	219.7636±7.85508	226.5636±5.3602
5	7 th Post-operation day	216.5273±7.0628	219.3818±5.8420
6	28 th Post-operation day	213.0727±7.1927	214.2727±7.1322
	(Signal strength)	Group 1	Group 2
7	Pre-operation day	6.4545±0.8567	5.6727±0.72148
8	7 th Post-operation day	7.8000±0.75523	9.00±7.7455
9	28 th Post-operation day	7.9815±0.85761	7.9273±0.6340

Table 4: Comparison of Macular Thickness (Centre) at different follow-up periods

Sr. No.	Parameter	Mean Thickness between Pre-Op & 7 day	Mean Difference between Pre-Op & 7 day	Mean Thickness between 7 day & 28 day	Mean Difference between 7 day & 28 day	Mean Thickness between Pre-Op & 28 day	Mean Difference between Pre-Op & 28 day
1	Group 1	218.50±11.16	2.24±7.90	217.51±7.93	4.22±7.38	216.39±9.50	1.98±11.18
2	Group 2	223.83±9.11	2.60±9.91	218.91±11.49	7.24±5.36	220.21±8.17	9.84±10.04
3	P Value*	0.043	0.003	0.834	0.006	0.084	0.000

*Mann Whitney test was applied

Table 5: Comparison of Macular Thickness (Cube) at different follow-up periods

Sr. No.	Parameter	Mean Thickness between Pre-Op & 7 day	Mean Difference between Pre-Op & 7 day	Mean Thickness between 7 day & 28 day	Mean Difference between 7 day & 28 day	Mean Thickness between Pre-Op & 28 day	Mean Difference between Pre-Op & 28 day
1	Group 1	218.14±7.32	3.23±3.00	21.80±6.94	3.45±3.28	216.42±7.23	6.70±4.20
2	Group 2	222.97±4.92	7.18±5.37	216.82±6.17	5.10±4.018	220.42±8.18	9.84±10.04
3	P Value*	0.001	0.000	0.181	0.049	0.006	0.000

*Mann Whitney test was applied

Discussion

Singh R and associates¹³ have studied the changes in macular thickness and visual acuity after cataract surgery with postoperative nepafenac in patients with diabetic retinopathy. In their research, the nepafenac group had a significantly lower central macular thickness as compared to the vehicle group. Our study yielded the same results in which the change in mean macular thickness (centre & cube) was more in the NSAID group and was statistically significant. Similarly, nepafenac group patients had a lower visual acuity decrease of more than five letters than the vehicle group.

Stock RA¹⁴ and colleagues compared the effects of nepafenac and ketorolac on macular thickness after cataract surgery. Their study yielded no difference between pre and post-operative macular thickness with the use of either drug or between the two groups. Almost similar results were reported by Ellakwa AF¹⁵ and associates who studied the efficacy of nepafenac eye drops in preventing post cataract surgery macular edema. Although this study revealed no statistically significant difference before and after the use of nepafenac and dexamethasone in separate groups, the researchers concluded that these drugs do have a prophylactic role in reducing the load of macular edema post cataract surgery. Similar results were noted in the current study in which the use of postoperative nepafenac leads to a statistically significant change in macular thickness although macular edema was documented.

Singh RP et al¹⁶ published the results of their randomized control trial in which they evaluated the efficacy of 0.3% nepafenac after cataract surgery in patients with diabetic retinopathy.

Fewer study subjects developed macular edema after cataract surgery when nepafenac eye drops were used along with as compared to controls. A similar trend was observed in relation to visual acuity improvement. Despite the current study being done on patients without diabetic retinopathy but its results are comparable to the above-mentioned trial conducted on patients with diabetic retinopathy. Another randomized control trial conducted by Pollack A¹⁷ and associates studied the efficacy of nepafenac at 0.1%. They concluded that a three-month use of nepafenac after cataract surgery helps prevent the development of macular edema without any safety concerns.

El Gharbway¹⁸ and colleagues studied the effect of nepafenac 0.1% eye drops after cataract surgery in patients (Glaucoma, uveitis, traumatic cataract) who

were at high risk of developing post-operative pseudophakic macular edema. The study suggests the use of topical nepafenac eye drops after cataract surgery in high-risk patients as it significantly reduces the incidence of macular edema in pseudophakic patients. The study showed a beneficial effect of using post-operative nepafenac in patients with coexisting ocular disease and its recommendations are similar to the results of the current study. Danni R et al¹⁹ went one step ahead and studied the use of pre-operative nepafenac and its impact on visual and macular thickness outcomes. It was found that pre-operative nepafenac does not improve the visual and macular thickness outcome after cataract surgery.

Campa C²⁰ and associates studied the benefits of adding either nepafenac or bromofenac to the post-operative steroid regimen and its impact on macular thickness. The study showed a lower incidence of pseudophakic macular edema when non-steroidal anti-inflammatory drugs were added to post-operative medication. Sahin AK²¹ and colleagues compared the effect of post-cataract surgery prednisolone versus prednisolone and nepafenac in preventing macular edema. Macular thickness in the combined steroid and non-steroidal anti-inflammatory drug group was less than in the other group hence depicting the efficacy. A randomized controlled trial conducted at Rawalpindi assessed the effect of post-operative nepafenac in halting the development of macular edema after phacoemulsification in patients with a non-proliferative stage of diabetic retinopathy. Macular edema was defined as a 10% increase in macular thickness from first contact. In this study, 23% of patients developed macular edema following surgery in the control group as compared to 3% in the nepafenac group.²²

A major limitation of this study is being a single centre study and having a relatively smaller sample size as cataract surgery is a routinely performed surgery. Authors suggest a multicentre trial on a larger sample and also taking into account other comorbidities in patient and their impact on macular thickness post-operatively.

Conclusion

Post-Operative NSAID leads to a better reduction of the macular thickness (less increase) after cataract surgery in diabetic patients without retinopathy.

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