

COMPARISON OF EFFICACY OF NEPAFENAC 0.3% & 0.1% TO PREVENT & CONTROL POSTOPERATIVE PAIN AND CONJUNCTIVAL REDNESS AFTER CATARACT SURGERY

SAIRA JABEEN¹, ZEESHAN HAMEED¹, BAZLA BATOOL¹, IRFAN QAYYUM MALIK¹,
AAMNA JABRAN¹, ABDULLAH YOUNAS²

¹Gujranwala Medical College/ DHQ Teaching Hospital, Gujranwala, ²Ibrahim Trust Eye Hospital, Gujranwala

ABSTRACT

Objectives: To compare the efficacy of nepafenac 0.3% with nepafenac 0.1% to control postoperative pain and conjunctival redness after cataract surgery.

Methods: It is a randomized controlled trial conducted at Ophthalmology Department, DHQ Teaching Hospital, Gujranwala from November 2020 to January 2021. A prospective review of 70 patients operated for age-related cataract was done. Patients were divided into two equal groups. Group A patients were given Ilevro eye drops (nepafenac 0.3%) once a day and group B patients were instilled Nevanac eye drops (nepafenac 0.1%) thrice a day. All patients were scored for ocular pain and conjunctival redness on basis of pre-defined scales on one day before surgery and on 1st, 7th and 14th postoperative day. Results from both groups were analyzed and compared using SPSS v 25.0.

Results: Out of 70 patients, 35 were put in group A and 35 into group B. Overall 37 (52.8%) patients were male and 33 (47.2%) were female. Patients above 40 years of age were 33 (94.3%) in group A and 35 (100%) in group B. Patients having pain score ≥ 5 were 30 (85.7%) in group A and 25 (71.4%) in group B on 1st postoperative day, with ≥ 3 were 1 (2.8%) in group A and 33 (94.2%) in group B at 7th postoperative day and zero on 14th postoperative day. Patients with conjunctival redness ≥ 2 were 31 (88.6%) in group A and 29 (82.9%) in group B on 1st postoperative day, with ≥ 1 were 18 (51.3%) in group A and 28 (79.9%) in group B on 7th postoperative day while four (11.4%) in group A and one (2.8%) in group B on 14th postoperative day.

Conclusion: Effect of once daily nepafenac 0.3% on postoperative pain and conjunctival redness was found to be sub-rated against thrice daily nepafenac 0.1% on 1st postoperative day. However, this effect became equal and then slightly superior to that of nepafenac 0.1% on 7th and 14th postoperative days.

Key Words: Cataract Surgery, Nepafenac, Postoperative Pain, Conjunctival Redness

How to cite this article: Hussain Y, Aslam S, Munawar N, Ain Q, Anjum R. Factors affecting nutritional vitamin D level in patients on maintenance hemodialysis. Pak Postgrad Med J 2021;32(3): 110-114

This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/3.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

DOI: <https://doi.org/10.51642/ppmj.v32i03.456>

*Correspondence to: Zeeshan Hameed
Postgraduate Resident Ophthalmology
Gujranwala Medical College/ DHQ Teaching Hospital,
Gujranwala, Pakistan.*

Email: zeeshanhameed097@gmail.com

INTRODUCTION

Cataract is formed by opacification of crystalline lens which affects visual acuity as it matures.¹ Cataract is

one of the most common causes of blindness which accounts for nearly 48% of global blindness.^{2,3}

Cataract surgery is one of the most easily assessable ophthalmic surgeries worldwide and thus a fairly commonly performed procedure in ophthalmology practice.⁴ There are many per-operative and post operative complications of this procedure. Post operative ocular inflammation is common after cataract surgery which causes postoperative pain and photophobia.⁵ Ocular inflammation can be due to

exogenous or endogenous factors. Exogenous factors include trauma and surgery. There are many complications associated with acute inflammation which include raised Intraocular pressure, inflammatory membrane, decreased visual acuity and cystoid macular edema etc.

As with other tissues, in ocular inflammation arachidonic acid metabolism produces prostaglandins by action of cyclooxygenase enzymes which are the most important mediators of inflammation. Surgical trauma is one of the main triggers of arachidonic acid metabolism. Ocular inflammation is manifested by redness, swelling and pain associated with irritation after surgical trauma to eyes.⁶

There are many topical medications used after cataract surgery including antibiotics, steroids, non-steroidal anti-inflammatory agents (NSAIDs) and anti-glaucoma drops to reduce risk of postoperative complications.⁷ Many surgeons use NSAIDs for providing best surgical outcomes in patients undergoing cataract surgery and in early post operative period to reduce surgical induced inflammation. NSAIDs are safe and effective alternative to steroids in reducing post operative pain and inflammation. They are also effective in maintaining intra-operative mydriasis.⁸

There are many different types of NSAIDs which are in clinical use for different purposes. Four topical NSAIDs currently approved for use by FDA for post operative pain and inflammation after cataract surgery are diclofenac sodium 0.1%, ketorolac 0.5% (used four times a day), nepafenac 0.1% three times a day and bromfenac twice a day.⁹

Recently a new drug formulation, nepafenac 0.3% is available with once-a-day dosing to serve the same purpose.

The rationale of this study is to compare the efficacy of 0.3% nepafenac given only once a day with 0.1% nepafenac given three times a day for controlling post operative pain and inflammation.

Methods:

This was a randomized control trial conducted at DHQ Teaching Hospital, Gujranwala from November 2020 to January 2021. This study was approved by Ethical Review Committee of above-mentioned hospital. Informed consent was taken from all the participants. A total of 70 patients were included in the study. They were selected randomly by simple random technique. They were divided into two groups. Group A included 35 patients who received nepafenac 0.3% (Ilevro Eye Drops, Alcon laboratories, Inc.) used only once a day while group B included 35 patients who received nepafenac 0.1% (Nevanac Eye Drops, Alcon laboratories, Inc.) three times a day. All patients in group A started nepafenac 0.3% one day before surgery, continued it twice a day on per op day in

patients 1 drop early morning and 1 drop of drug half hour before surgery and continued in once daily dose for 14 days post operatively. Patients in group B were given nepafenac 0.1% three times a day, one day pre-operatively and continued for 14 days postoperatively. All the patients were 35 years or older, having age-related cataracts and underwent phacoemulsification surgery for cataract extraction. Patients having traumatic cataracts, complicated cataracts, patients with severe retinal pathologies and who had poor surgical outcomes based on per-operative evaluation were excluded from the study. The study was conducted to find out effect of nepafenac 0.3% versus nepafenac 0.1% in controlling pain and redness after cataract surgery.

Pain was assessed on commonly used pain score criteria in which patients rated their pain on a scale of 0 to 10. Zero meant no pain and 9 or 10 meant worst possible pain. Following is table given for pain assessment. (Taken from <https://www.pinterest.com/pin/691795192749246549/>)

Pain Severity Scale

Severity	Description
10 Unable to Move	I am in bed and can't move because of my pain. I need someone to take me to the emergency room.
9 Severe	My pain is all that I can think about. I can barely talk or move because of the pain.
8 Intense	My pain is so severe that it is hard to think of anything else. Talking and listening are difficult.
7 Unmanageable	I am in pain all of the time. It keeps me from starting most activities.
6 Distressing	I think about my pain all of the time. I have to stop during most activities because of my pain.
5 Distracting	I think about my pain most of the time. I cannot do some activities because of my pain.
4 Moderate	I am constantly aware of my pain but I can continue most of my activities.
3 Uncomfortable	My pain bothers me but I can ignore it most of the time.
2 Mild	I have a low level of pain. I am aware of my pain only when I pay attention to it.
1 Minimal	My pain is hardly noticeable.
0 No Pain	I have no pain.

Conjunctival redness was described as follows. Diffuse conjunctival injection scored as 3, moderate redness scored as 2 and mild redness to no injection as 1. Pain and redness were two outcome variables noted preoperatively, on 1st post operative day, 7th post operative and 14th post operative day. Results of both study groups were analyzed and compared using SPSS v 25.0.

RESULTS

Total patients included in the study were 70 (n=70) out of which 37 (52.8%) were male and 33 (47.2%) were female. For the sake of comparison, patients were divided into two groups. Group A included 35 patients who received Ilevro (nepfenac 0.3%) eye drops used only once a day. Group B included 35 patients who received Nevanac (nepafenac 0.1%) eye drops three times a day. In group A, out of 35, 18 (51.4%) were male and 17 (48.6%) were female. In group B, 19 (54.3%) were male and 16 (45.7%) were female. (Table 1)

Table 1: Frequency Distribution of Gender

Gender	Group A (n=35)	Group B (n=35)
Male	18 (51.4%)	19 (54.3%)
Female	17 (48.6%)	16 (45.7%)
Total	35 (100%)	35 (100%)

In age groups, patients aged 40 years or less were 2 (5.7%) in group A and 0 (0%) in group B. Patients

Table 3: Frequency Distribution of Pain Score in Both Groups

Pain Score	Pain Score at 1 st Postoperative Day		Pain Score at 7 th Postoperative Day		Pain Score at 14 th Postoperative Day	
	Group A (n=35)	Group B (n=35)	Group A (n=35)	Group B (n=35)	Group A (n=35)	Group B (n=35)
1-10						
>6	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
6	7 (20%)	7 (20%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
5	23 (65.7%)	18 (51.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
4	5 (14.3%)	8 (22.8%)	0 (0%)	17(48.5%)	0 (0%)	0 (0%)
3	0 (0%)	2 (5.6%)	1(2.8%)	16(45.7%)	0 (0%)	0 (0%)
<3	0 (0%)	0 (0%)	34(97.1%)	2(5.7%)	35 (100%)	35 (100%)
Total	35 (100%)	35 (100%)	35 (100%)	35 (100%)	35 (100%)	35 (100%)

Table 4: Frequency Distribution of Conjunctival Redness in Both Groups

Redness Score 0-3	Conjunctival Redness at 1 st Postoperative Day		Conjunctival Redness at 7 th Postoperative Day		Conjunctival Redness at 14 th Postoperative Day	
	Group A (n=35)	Group B (n=35)	Group A (n=35)	Group B (n=35)	Group A (n=35)	Group B (n=35)
3	5(14.3%)	5 (14.3%)	0 (0%)	0(0%)	0 (0%)	0 (0%)
2	26(74.3%)	24(68.6%)	3(8.5%)	3(8.5%)	0 (0%)	0 (0%)
1	4(11.4%)	6(2.8%)	15(42.8%)	25(71.4%)	4(11.4%)	1(2.8%)
0	0(0%)	0(0%)	17 (48.5%)	7 (20%)	31(88.5%)	34(97.2%)
Total	35 (100%)	35 (100%)	35 (100%)	35 (100%)	35 (100%)	35 (100%)

DISCUSSION

In this study 52.8% of patients were male and 47.2% were female. Mean age was above 32 years of age. All patients having nuclear cataract¹⁰ undergoing phacoemulsification cataract surgery were planned for our study.

between age of 41-60 years were 23 (65.7%) in group A and 13 (37.1%) in group B. Patients above age of 60 were 10 (28.5%) in group A and 22 (62.9%) in group B. (Table 2)

Table 2: Frequency Distribution of Age Groups

Age (years)	Group A (n=35)	Group B (n=35)
≤40	2 (5.7%)	0 (0%)
41-60	23 (65.7%)	13 (37.1%)
>60	10 (28.5%)	22 (62.9%)
Total	35 (100%)	35 (100%)

As implied above, the comparative efficacy of both drug groups was noted in terms of pain as well as redness at 1 day before surgery, at 1st postoperative day, 7th postoperative day and on 14th postoperative day. Obviously, no group had any pain or redness at 1 day before surgery. However, on rest of occasions following results were documented. (Table 3,4)

For post-operative management of pain and inflammation topical steroids, topical and systemic non-steroidal anti-inflammatory drugs¹¹ are available and literature shows satisfactory control of pain and inflammation with them.

In our study pre surgery pain and inflammation has been recorded that was zero in both groups. Taking in

account the anti-inflammatory role of nepafenac¹² as it inhibits the release the prostaglandins literature shows various studies for the affectivity of NSAIDs¹³ in the management of post-operative inflammation.

History also shows the role of NSAIDs in control of CSME^{14,15}, diabetes induced retinal microvascular disease¹⁶, in management of intraocular pressure¹⁷, control of inflammation in extra ocular surgery.¹⁸

For the analgesic effect of NSAIDs literature shows studies that compare topical NSAIDs with topical steroids¹⁹ or history shows comparison of NSAIDs²⁰ or combination with ketorolac²¹, showing that NSAIDs are equivalent to or superior to other topical or placebo²² management.

In our study we compare two different strengths of NSAIDs 0.1% vs. 0.3%. it showed that majority of group 'B' patients experience pain score of 5 at 1st post-operative day that is 51.4%, while majority of group 'A' patients receiving 0.3% of topical NSAIDs also experience pain score of 5 at 1st post-operative day in 65.7% of patients.

While on 7th post-operative day patients of group 'B' experience pain of grade 4 in 48.5% of patients, while in group 'A' 97.1% of patients experience pain of <3 score that is much reduced as compare to group 'B' and is in correspondence with literature review. On 14th post-operative day both 0.1% and 0.3% NSAIDs are equivalent in terms of pain that is <3 pain score.

Grade 2 conjunctival redness was mostly experienced by patient on 1st post-operative day out of which 68.6% was experienced by group 'B' and 74.35 was experience by group 'A'. while on follow up at 7th and 14th post op day group 'A' patients shows marked decrease in conjunctival redness (42.8% and 88.5%) as compare to group 'B' (71.4% and 97.2 %) respectively, this shows that nepafenac 0.3% is better in management of pain and inflammation^{23,24} at 14 days follow-up.

This study is limited by relatively small size for comparison and short duration of follow-up although literature shows no study showing the comparison of nepafenac 0.1% vs. nepafenac 0.3%.

CONCLUSION

Effect of nepafenac 0.3% once daily dropping in terms of controlling postoperative pain and conjunctival redness is not superior as compared to nepafenac 0.1% thrice daily dropping on 1st postoperative day. However, this effect becomes equal and then slightly superior to that of nepafenac 0.1% on 7th and 14th postoperative days after cataract surgery concluding that nepafenac 0.1% given 3 times daily offers more control of pain and redness in early postoperative days while same is true about nepafenac 0.3% given once a day after 1-2 weeks.

CONFLICT OF INTERESTS

Authors declared no conflict of interests.

FUNDING

No funding was provided for this study.

ETHICAL APPROVAL

The study was approved by the Institutional review board/ Ethical review committee of Gujranwala Medical College/ DHQ Teaching Hospital, Gujranwala. Vide IRB Reference No. 382/GMC.

REFERENCES

1. Grulkowski I, Manzanera S, Cwiklinski L, Mompeán J, De Castro A, Marin JM, et al. Volumetric macro-and micro-scale assessment of crystalline lens opacities in cataract patients using long-depth-range swept source optical coherence tomography. *Biomedical optics express*. 2018 Aug 1;9(8):3821-3833.
2. Kisa A, Bourne RR, Steinmetz JD, Briant PS, Flaxman SR, Kisa S, et al. Causes of blindness and vision impairment in 2020 and trends over 30 years, and prevalence of avoidable blindness in relation to VISION 2020: the Right to Sight: an analysis for the Global Burden of Disease Study.
3. Ahmed M, Beletew B, Mengesha A, Markos M. Prevalence of cataract and its associated factors among adults aged 40 years and above in Waghimra zone, Amhara, Northeast Ethiopia: A Community based cross-sectional study.
4. Tan AG, Kifley A, Tham YC, Shi Y, Chee ML, Sabanayagam C, et al. Six-year incidence of and risk factors for cataract surgery in a multi-ethnic Asian population: the Singapore Epidemiology of Eye Diseases Study. *Ophthalmology*. 2018 Dec 1;125(12):1844-1853.
5. Lane SS, Modi SS, Lehmann RP, Holland EJ. Nepafenac ophthalmic suspension 0.1% for the prevention and treatment of ocular inflammation associated with cataract surgery. *Journal of Cataract & Refractive Surgery*. 2007 Jan 1;33(1):53-58.
6. Cho H, Wolf KJ, Wolf EJ. Management of ocular inflammation and pain following cataract surgery: focus on bromfenac ophthalmic solution. *Clinical ophthalmology (Auckland, NZ)*. 2009; 3:199.
7. Erichsen JH, Forman JL, Holm LM, Kessel L. Effect of anti-inflammatory regimen on early postoperative inflammation after cataract surgery. *Journal of Cataract & Refractive Surgery*. 2021 Mar 1;47(3):323-330.
8. Hoffman RS, Braga-Mele R, Donaldson K, Emerick G, Henderson B, Kahook M, et al. Cataract surgery and nonsteroidal anti-inflammatory drugs. *Journal of Cataract & Refractive Surgery*. 2016 Sep 1;42(9):1368-1379.

9. Cagini C, Pellegrino A, Cerquaglia A, Iaccheri B, Lupidi M, Fiore T. Comparison of the effect of diclofenac 0.1% and nepafenac 0.1% on aqueous flare in patients undergoing cataract surgery: a prospective randomized study. *Current eye research*. 2020 Sep 1;45(9):1089-1093.
10. Truscott RJ, Friedrich MG. Molecular processes implicated in human age-related nuclear cataract. *Investigative ophthalmology & visual science*. 2019 Dec 2;60(15):5007-5021.
11. Rizzo S, Gambini G, De Vico U, Rizzo C, Kilian R. A One-Week Course of Levofloxacin/ Dexamethasone Eye Drops: A Review on a New Approach in Managing Patients After Cataract Surgery. *Ophthalmology and Therapy*. 2021 Dec 22:1-1.
12. Kaduševičius E. Novel Applications of NSAIDs: Insight and Future Perspectives in Cardiovascular, Neurodegenerative, Diabetes and Cancer Disease Therapy. *International Journal of Molecular Sciences*. 2021 Jan;22(12):6637.
13. Kessel L, Tendal B, Jørgensen KJ, Erngaard D, Flesner P, Andresen JL, et al. post-cataract prevention of inflammation and macular edema by steroid and nonsteroidal anti-inflammatory eye drops: a systematic review. *Ophthalmology*. 2014 Oct 1;121(10):1915-1924.
14. Aaronson A, Achiron A, Tuuminen R. Clinical course of pseudophakic cystoid macular edema treated with nepafenac. *Journal of clinical medicine*. 2020 Sep;9(9):3034.
15. Warren KA, Fox JE. Topical nepafenac as an alternate treatment for cystoid macular edema in steroid responsive patients. *Retina*. 2008 Nov 1;28(10):1427-1434.
16. Kern TS, Miller CM, Du Y, Zheng L, Mohr S, Ball SL, et al, Bingaman DP. Topical administration of nepafenac inhibits diabetes-induced retinal microvascular disease and underlying abnormalities of retinal metabolism and physiology. *Diabetes*. 2007 Feb 1;56(2):373-379.
17. Dave P, Shah K, Ramchandani B, Jain R. Effect of nepafenac eye drops on intraocular pressure: a randomized prospective study. *American journal of ophthalmology*. 2014 Mar 1;157(3):735-738.
18. Ozcimen M, Sakarya Y, Goktas S, Sakarya R, Yener HI, Bukus A, Demir LS. Effect of nepafenac eye drops on pain associated with pterygium surgery. *Eye & contact lens*. 2015 May 1;41(3):187-189.
19. Sarkar S, Bardoloi N, Deb AK. Comparison between 0.1% Nepafenac and 1% Prednisolone Eye Drop in Postoperative Management Following Micro-Incisional Cataract Surgery. *Korean journal of ophthalmology: KJO*. 2021 Jun;35(3):188.
20. Almeida DR, Khan Z, Xing L, Bakar SN, Rahim K, Urton T, et al. Prophylactic nepafenac and ketorolac versus placebo in preventing postoperative macular edema after uneventful phacoemulsification. *Journal of Cataract & Refractive Surgery*. 2012 Sep 1;38(9):1537-1543.
21. Coassin M, Iovieno A, Soldani A, Cavuto S, Cimino L, Sartori A, et al. Bromfenac ophthalmic solution 0.09% as an adjunctive therapy to topical steroids after cataract surgery in pseudo exfoliation syndrome. *Journal of Cataract & Refractive Surgery*. 2016 Aug 1;42(8):1119-1125.
22. Nardi M, Lobo C, Bereczki A, Cano J, Zagato E, Potts S, et al. Analgesic and anti-inflammatory effectiveness of nepafenac 0.1% for cataract surgery. *Clin Ophthalmol*. 2007 Dec;1(4):527-33. PMID: 19668532; PMCID: PMC2704522.
23. Jones BM, Neville MW. Nepafenac: An Ophthalmic Nonsteroidal Antiinflammatory Drug for Pain After Cataract Surgery. *Annals of Pharmacotherapy*. 2013;47(6):892-896. doi:10.1345/aph.1R757
24. Modi SS, Lehmann RP, Walters TR, Fong R, Christie WC, Roel L, et al. Once-daily nepafenac ophthalmic suspension 0.3% to prevent and treat ocular inflammation and pain after cataract surgery: phase 3 study. *Journal of Cataract & Refractive Surgery*. 2014 Feb 1;40(2):203-211.

AUTHOR'S CONTRIBUTIONS

SJ, BB: Manuscript Writing, Data collection

ZH: Manuscript Writing, Statistical Analysis, Correspondence

IQM, AJ, AY: Supervision, Manuscript Review