ROLE OF NEPAFENAC 0.03% IN MAINTAINING MYDRIASIS DURING CATARACT SURGERY

Dr. Mona Liza Mahesar, Dr. Noman Ahmed Shaikh

Institute of Ophthalmology

Liaquat University of Medical and Health Sciences Jamshoro

Abstract

Background:

To ensure the best post-procedure outcomes after simple or complex cataract surgery ophthalmic surgeons prescribe topical non-steroidal anti-inflammatory medications (NSAIDs), to improve patient compliance, nepafenac 0.3% was approved in October 2012 and has been demonstrated to have equivalent efficacy to the 0.1% solution with only a once-daily administration.

Methodology:

This is a retrospective, case-control study of 90 patients, 45 in the case group and 45 in the control group. All patients were evaluated pre-operatively for vision impairments, associated issues, comorbidities, and other exclusion criteria factors. A similar standardized method was used for surgery incision and pupil measurements to eliminate biases. The data were assembled in Microsoft Excel and analyzed using Statistical Package of Social Sciences (version 22).

Results:

The overall mean age of study participants was 54.2 ± 3.8 years. Reported associated pathology diabetes mellitus was reported in 68.8% of the cases group, while upon categorizing it with or without diabetic retinopathy the cases group showed 31.1% and 37.7% frequency respectively. Overall comparison of the mean value of pupil size has indicated a prominent difference in pupil size after surgery in the cases group with a significant p-value of 0.02, indicating higher efficacy of nepafenac 0.3%. In both groups, diabetic patients' measurements were greater than non-diabetic patients' measurements, without statistically significant differences. There was no clinically significant vision loss in any of the patients.

Conclusion:

The use of nepafenac 0.3% as a preventive measure during cataract surgery was successful and safe in maintaining mydriasis and minimizing postoperative macular edema. A once-daily regimen of 0.3% concentration is no worse than a three-times-daily regimen of 0.1% concentration, resulting in higher patient compliance.

Keywords:

Nepafenac 0.3%, cataract surgery, Mydriasis.

Introduction:

Cataracts are known as the major cause of blindness and visual impairment worldwide, one of the most often performed procedures in the world, cataract surgery is also one of the most effective medical treatments [1]. Regardless of developments in surgical methods and equipment, cataract surgery may still provoke an inflammatory reaction that, if left untreated, might result in major side effects such as higher intraocular pressure and diabetic macular edema (CME), which would eventually weaken vision[2]. To ensure the best post-procedure outcomes after simple or complex cataract surgery ophthalmic surgeons prescribe topical non-steroidal anti-inflammatory medications (NSAIDs), either alone or in combination with steroid drops to reduce intraoperative and postoperative ocular discomfort, inflammation, CME, and support intraoperative mydriasis. From the list of available NSAIDs, nepafenac is known to convert into amfenac after application and has exceptional corneal penetration[3]. Nepafenac 0.1% has been demonstrated to be beneficial in lowering the chance of developing postoperative CME in diabetic patients, and it was approved in 2005 for the therapy of postoperative pain, inflammation, and CME following simple and difficult cataract surgery [4-6]. Additionally, to improve patient compliance, nepafenac 0.3% was approved in October 2012 and has been demonstrated to have equivalent efficacy to the 0.1% solution with only a once-daily administration [7-8].

This study aims to provide a comprehensive view of using nepafenac 0.3% intraoperative to reduce mydriasis after cataract surgery and evaluate the determinants of mydriasis by comparing cases and control groups. To the best of our knowledge, this is the first study to assess the effect of nepafenac 0.3% in the Pakistani population intraoperatively.

Methodology:

Study design:

This is a retrospective, case-control study that included patients undergoing cataract surgery in the ophthalmology department of Liaquat University of medical and health sciences, jamshoro from January 2022 to December 2022.

Patients and methodology:

After getting ethical approval from the institutional review board, 90 patients were included in the study, 45 in the case group and 45 in the control group. The stratification of cases and controls was determined by similar demographic aspects including sex, age, and associated disorder. The inclusion criteria were adult patients age ranging from 18 to 60 years with a confirmed diagnosis of senile and/or metabolic cataract (according to the Lens Opacities Classification System LOCS III, with classification NO and NC 2–3). The cases group patients were administered nepafenac 0.03% during surgery while the control group patients didn't have nepafenac 0.3%. Both groups were evaluated for post-operative mydriasis and results were compared to assess the efficacy of nepafenac 0.3% during surgery. However, pregnant females, breastfeeding mothers, ocular inflammation, or positive history of eye infection 1 month before surgery, and any history of eye medication usage including drops or NSAIDs were excluded from the study. Uncontrolled diabetes mellitus (DM), blood glucose levels (> 126 mg), proliferative diabetic retinopathy, and/or

macular edema, synechiae, ocular alteration preventing adequate mydriases such as iris atrophy, macular alteration documented by optical coherence tomography (OCT), including macular edema of any etiology, macular holes, epiretinal membrane, macular degeneration related to age, and central serous chorioretinopathy and the use of contact lens in the eye involved during the study were also considered exclusion criteria.

Study Protocol:

All patients were evaluated pre-operatively for vision impairments, associated issues, comorbidities, and other exclusion criteria factors. A similar standardized method was used for surgery incision and pupil measurements to eliminate biases. Follow-up measurements of the treated pupil were taken after surgery and the day after surgery before discharge to access the difference between nepafenac 0.3% solution.

Statistical analysis

The data were assembled in Microsoft Excel and analyzed using Statistical Package of Social Sciences (version 22). Data from patients in the nepafenac and control groups were described as mean values and proportions and were compared by using the ANOVA or Student's *t*-test. The Fisher exact test was used to associate the qualitative variables and to determine the relative risk. Statistical significance was established at a p-value of <0.05. The demographic data included age, gender, and evaluated eye, while the clinical data included the presence or absence of diabetes mellitus (without diabetic retinopathy, and the status of non-proliferative diabetic retinopathy), systemic arterial hypertension, and heart disease. The demographic data were compiled and compared between the two groups.

Results:

A total of 90 patients were enrolled in cases and control groups with 45 in each group respectively. The overall mean age of study participants was 54.2 ± 3.8 years while the control group mean age was 51.7 ± 5.2 and 52.4 ± 4.7 and the range was measured as 47 to 65 and 45 to 65 respectively, while the p-value was 0.57. Gender distribution between cases and control groups was 57.7% and 31.1% of male participants and 42.2% and 68.8% of female participants respectively. The laterality of affected eyes was reported as the right side of 37.7% in the control group and 51.1% in the cases group, and similarly left eye was reported in 62.2% and 48.8% in the control group.

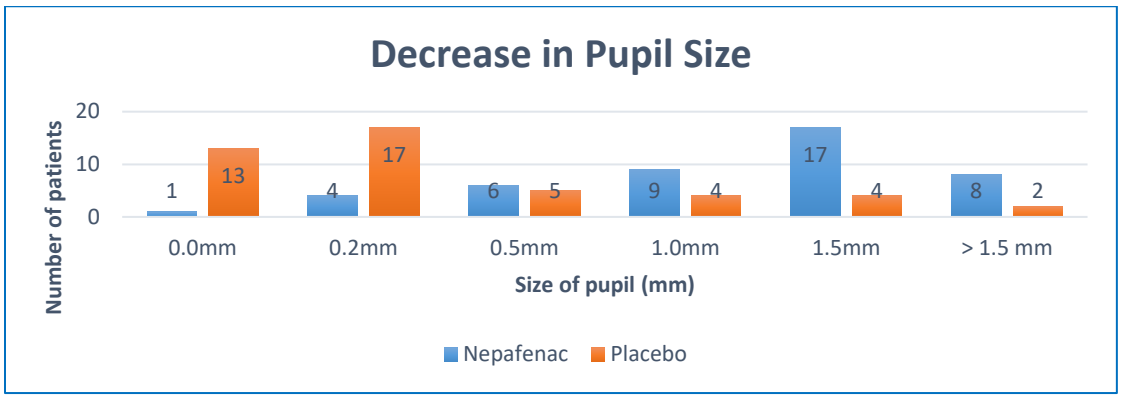
Reported associated pathology diabetes mellitus was reported in 68.8% of the cases group, while upon categorizing it with or without diabetic retinopathy the cases group showed 31.1% and 37.7% frequency respectively. Hypertension was reported in 91.1% while the cardiovascular disease was in 60% of cases participants. Only significant p-value was reported for gender distribution with 0.01. (Table 01

Table 01: Phacoemulsification with Intraocular lens implantation

Variables	Control (n=45)	Nepafenac 0.3% (n=45)	P-Value
Age (Years)			
Mean ± SD	51.7 ± 5.2	52.4 ± 4.7	0.57
Range	47 to 65	45 to 65	
Gender			
Male	26 (57.7%)	14 (31.1%)	0.01
Female	19 (42.2%)	31 (68.8%)	
Eye			
Right eye	17 (37.7%)	23 (51.1%)	0.72
Left eye	28 (62.2%)	22 (48.8%)	
Pathology			
DM	29 (64.4%)	31 (68.8%)	0.24
With DR	19 (42.2%)	14 (31.1%)	0.71
Without DR	10 (22.2%)	17 (37.7%)	0.47
HTN	38 (84.4%)	41 (91.1%)	0.66
CVD	21 (46.6%)	27 (60%)	0.52

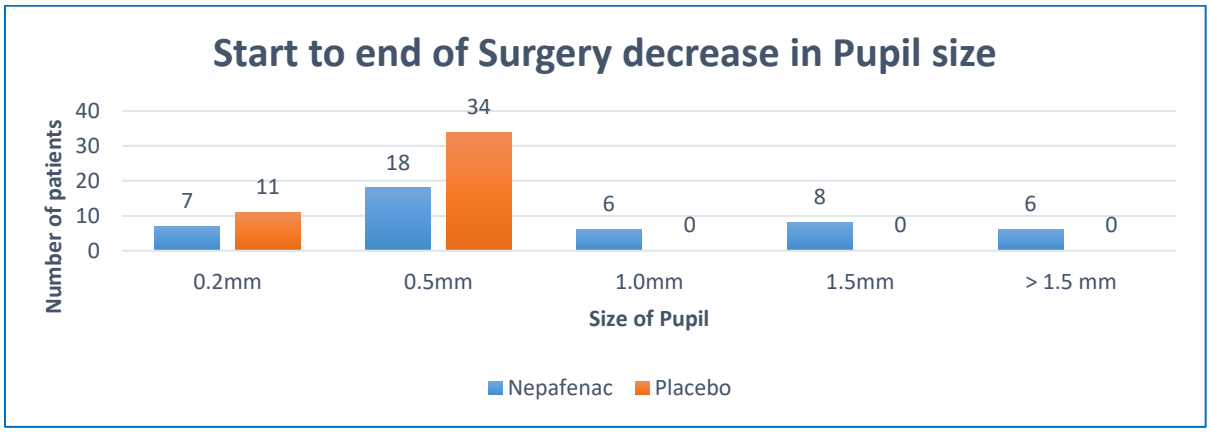
Measurement of pupil size before and after surgery was reported in both groups, the size was categorized as no difference (0.0mm), the minimal difference with 0.2mm – 0.5mm), a good difference (1.0mm) and excellent difference (1.5mm and > 1.5mm) indicating higher rates of no difference to minimal difference of pupil size in the control group with 13 (28.8%) and 17 (37.7%) patients from control group indicating no difference while only 1(2.2%) and 4(8.8%) from cases group reported no difference to minimal difference respectively. However, good difference categories were similar or higher in cases groups with 6 (13.3%) and 9 (20%) with 0.5mm and 1.0mm size differences respectively. Excellent difference of 1.5mm to > 1.5mm was comparatively higher in cases group with 17 (37.7%) and 8 (17.7%) with 1.5mm and > 1.5mm respectively. (Figure 1)

Figure 1: Estimation of pupil size decrease before and after surgery in case and control groups.



To assess the overall pupil size difference from the start to the end of surgery a significant difference has been noted in the cases group with all patients reporting excellent size decrease of 0.2mm to >1.5mm in 7(15.5%), 18(40%), 6(13.3%), 8 (17.7%) and 6(13.3%) patients respectively, however, in control groups, the maximum number of patients reported 0.5mm decrease in 34(75.5%) patients. (Figure 2)

Figure 2: estimation of start-to-end decrease of pupil size in cases and control groups.



The mean before surgery pupil size in the cases group was 4.7 ± 0.4mm while during surgery it was 7.6 ± 0.2mm, after surgery measurements reported 5.7 ± 0.4mm while in control groups the reported mean value was 4.3 ± 0.4mm, 5.3 ± 0.6mm and 3.7 ± 1.3mm respectively. Overall comparison of the mean value of pupil size has indicated a prominent difference in pupil size after surgery in the cases group with a significant p-value of 0.02, indicating higher efficacy of nepafenac 0.3%. (Table 02)

Table 02: overall mean value of pupil size in cases and control groups.

Variables		Controls (n=45)	Nepafenac 0.3% (n=45)	P-Value
Pupil size	Before Surgery	4.37 ± 0.4	4.70 ± 0.4	0.21
	Surgery day	5.37 ± 0.6	7.65 ± 0.2	0.07
	After surgery	3.73 ± 1.3	5.7 ± 0.4	0.02

Furthermore, these characteristics were studied about diabetes, and it was clear that in both groups, diabetic patients' measurements were greater than non-diabetic patients' measurements, without statistically significant differences. There was no clinically significant vision loss in any of the patients. (Table 03)

Table 03: Total difference concerning diabetes mellitus

Variables	Time point	Diabetes mellitus		P-value
		Yes	No	
Control	Before surgery	0.21 ± 0.11	0.20 ± 0.06	0.18
	Surgery day	0.29 ± 0.27	0.21 ± 0.14	0.28
	After Surgery	0.22 ± 0.22	0.23 ± 0.18	0.34
Nepafenac 0.3%	Before surgery	0.12 ± 0.01	0.03 ± 0.23	0.42
	Surgery day	0.04 ± 0.20	0.02 ± 0.24	0.28
	After Surgery	0.09 ± 0.26	0.06 ± 0.21	0.14

Discussion:

Prostaglandins, among other things, play an essential part in the response to ocular trauma (including surgical trauma), generating inflammation, discomfort, trans-operative miosis, elevated IOP, and pseudophakic CME. Nepafenac 0.3% is a novel NSAID prodrug that is hydrolyzed in the intraocular tissues to amfenac, a powerful inhibitor of COX-1 and COX-2 enzymes and consequently an inhibitor of PG production [9]. It has also shown greater penetration of intraocular tissues, with sufficient quantities in the posterior portion to prevent PG production. NSAIDs have been shown in numerous studies to be effective medications for sustaining trans-operative mydriasis as well as avoiding and treating pseudophakic CME. The current study found that topical nepafenac 0.3% prevents miosis during cataract surgery[10]. In comparison to the control group, the nepafenac group consistently showed a tendency toward higher pupillary diameter during the various stages of surgery, with the latter decreasing mostly during phacoemulsification of the lens nucleus. Throughout the surgical procedure, a gradual inability to sustain mydriasis was noted in the control group. Because it interferes with the actual antimicrobial activity of the NSAIDs tested, intracameral epinephrine was not utilized in the irrigation solution in this investigation. A researcher's group

investigated the anti-miosis impact of topical prednisolone against flurbiprofen. Although there were no statistically significant differences between the two medicines, flurbiprofen caused more mydriasis [11-12]. It has also been found that using ketorolac three days before surgery is more successful than using it one day and one hour before surgery. In this trial, nepafenac was given one day before surgery, however, whether giving it three days before surgery will make a difference in the outcomes should be investigated in the future [13-14]. The prophylactic use of nepafenac 0.3% for preserving mydriasis during cataract surgery, as well as the behavior of postoperative macular thickness, has not previously been documented; nonetheless, significant outcomes in both areas were obtained in this study. More research with bigger sample sizes comparing nepafenac to other NSAIDs is needed [15-17].

Nepafenac safety profile:

Because their systemic absorption is low, NSAIDs have not been observed to induce systemic side effects. Burning, stinging, conjunctival hyperemia, and allergic contact dermatitis are the most commonly reported topical side effects, although superficial punctate keratitis, subepithelial infiltrates and immune rings, stromal infiltrates, epithelial abnormalities, and corneal ulceration have also been observed. Notably, the presence of an epithelial defect has been identified as the most prevalent cause of serious corneal damage; thus, patients with pre-existing corneal diseases that may predispose them to certain difficulties during NSAIDS treatment must be considered before beginning medication. Corneal denervation, corneal epithelial abnormalities, diabetes, contact lens wear, rheumatoid arthritis, rosacea, substantial dry eye illness, and usage of other keratotoxic drugs are examples of such disorders. Nepafenac's safety profile has been evaluated in multiple studies, with no significant adverse events reported in patients who had cataract surgery, whether they had pre-existing risk factors or not. Kawahara also evaluated the effects of topical nepafenac 0.1% and diclofenac 0.1% on the cornea, tear film, and ocular surface following standard cataract surgery. They discovered that diclofenac had considerably higher four weeks postoperatively than nepafenac, implying that the latter is safe for the corneal epithelium following standard cataract surgery [18-21].

Nepafenac and intraoperative mydriasis:

Maintaining intraoperative mydriasis is critical in attaining favorable postoperative outcomes in cataract surgery because the incidence of problems, such as posterior capsular tears, decreases dramatically. Several studies have demonstrated that topical NSAIDs, particularly nepafenac, can help to maintain intraoperative mydriasis during cataract surgery. One drop three times a day for 1-2 days before surgery and four times every half hour on the day of operation appears to be the appropriate dosing regimen for nepafenac 0.1%. It is worth noting that the researcher discovered no difference in maintaining intraoperative mydriasis between nepafenac 0.1% and ketorolac tromethamine 0.4% [22-24].

Nepafenac 0.1% vs. 0.3%:

Nepafenac topical suspension is available in doses of 0.1 and 0.3%. The first has been used three times a day, whilst the second has only been used once daily, contributing to higher

patient compliance and comfort with equal efficacy in both animal tests and clinical trials. The study directly compared two nepafenac concentrations to a placebo in avoiding and managing ocular pain and inflammation after cataract surgery. They found no significant difference between the 0.1% and 0.3% suspensions commencing one day before surgery and continuing for two weeks postoperatively, but both were superior to placebo. Furthermore, these concentrations have been shown in several studies to successfully minimize the prevalence of postoperative CME, as well as postoperative ocular pain and inflammation after cataract surgery [25-26].

Nepafenac versus other NSAIDs:

Nepafenac rapidly penetrates the cornea and sclera and is converted to its active metabolite, amfenac, mostly in the chorioretinal, iris, and ciliary body within the eye. Amfenac is a potent inhibitor of the COX-1 and COX-2 enzymes, which catalyze the formation of prostaglandins. After topical treatment, nepafenac reaches the posterior eye segment. The posterior distribution of nepafenac shows that it is active for a long time within vascularized tissues. In terms of comparing nepafenac to other NSAIDs, studies indicate that nepafenac is superior to other NSAIDs in managing postoperative inflammation, pain, and CME following cataract surgery, with fewer adverse effects [27].

The study examined the aqueous humor concentrations and COX-1/COX-2 inhibitory action of nepafenac, amfenac, ketorolac, and bromfenac and found that nepafenac had the shortest time to peak concentration and the greatest peak aqueous humor concentration, which was significantly higher than that of the other drugs, concluding that nepafenac has significantly greater ocular bioavailability than ketorolac and bromfenac. Furthermore, nepafenac 0.1% has been proven to be much more efficient than flurbiprofen 0.03% in preventing intraoperative miosis during conventional short-incision cataract surgery, however, a study found no difference in intraoperative mydriasis between nepafenac 0.1% and ketorolac 0.4%. On the other hand, research has shown that nepafenac is not superior to other NSAIDs [28].

Conclusion:

The use of nepafenac 0.3% as a preventive measure during cataract surgery was successful and safe in maintaining mydriasis and minimizing postoperative macular edema. A once-daily regimen of 0.3% concentration is no worse than a three-times-daily regimen of 0.1% concentration, resulting in higher patient compliance. According to a study of the literature, nepafenac plays a crucial effect in minimising postoperative CME development in high-risk patients, such as those with diabetes mellitus. However, the clinical indication in low-risk patients remains uncertain due to studies with contradictory results, despite the majority of studies reporting lower occurrence of postoperative inflammation and CME in patients treated with prophylactic topical nepafenac, even in the absence of risk factors for postoperative CME development.

References:

1. Kiziltoprak H, Koc M, Yetkin E, Tekin K, Inanc M, Ozulken K. Additive Effect of Topical Nepafenac on Mydriasis in Patients With Diabetes Mellitus. Eye & Contact Lens. 2020 Sep 1;46(5):310-3.
2. Cervantes-Coste G, Sánchez-Castro YG, Orozco-Carroll M, Mendoza-Schuster E, Velasco-Barona C. Inhibition of surgically induced miosis and prevention of postoperative macular edema with nepafenac. Clinical ophthalmology (Auckland, NZ). 2009;3:219.
3. Surhio SA, Memon M, Talpur R, Talpur KI. Efficacy of nepafenac 0.1% in maintaining mydriasis during phacoemulsification surgery. Jlumhs. 2013 May 1;12(02):74.
4. Sethi S, Chalia D, Chalia M, Kaur M. A study on effect of pre-operative topical prednisolone acetate, nepafenac and placebo, on intraoperative mydriasis and its sustenance during cataract surgery: a randomized trial.
5. Kızıltoprak H, Koç M, Yetkin E, Tekin K, İnanç M, Özülken K. Additive Effect of Topical Nepafenac on Mydriasis in Patients With Diabetes Mellitus. Eye & contact lens. 2020.
6. Bezatis A, Georgou I, Dedes J, Theodossiadis P, Chatziralli I. Nepafenac in cataract surgery. Clinical and Experimental Optometry. 2022 Apr 3;105(3):263-7.
7. Zhao X, Xia S, Wang E, Chen Y. Comparison of the efficacy and patients' tolerability of Nepafenac and Ketorolac in the treatment of ocular inflammation following cataract surgery: A meta-analysis of randomized controlled trials. PloS one. 2017 Mar 2;12(3):e0173254.
8. Prasad R, Bandyopadhyay A, Tiwari D, Singh B. Nepafenac vs bromfenac: A comparative study to determine their role in maintaining mydriasis during cataract surgery. inflammation.;10:14.
9. Sabbagh MT, Rajab M, Jalloul K. Study of the effect of adding topical Nepafenac 0.1% eye drop on increasing mydriasis in patients with diabetes mellitus type 2 : دراسة فعالية إضافة قطرة النيبافيناك الموضعي 0.1% في زيادة توسع الحدقة لدى مرضى الداء السكري النمط 2. مجلة العلوم الطبية و الصيدلانية. 2022 Mar 27;6(1):74-81.
10. during Small DI. Effect of Preoperative Use of Nepafenac and Flurbiprofen Eye Drops In Maintaining Mydriasis during Small Incision Cataract Surgery.
11. Jha R, Sur V, Bhattacharjee A, Ghosh T, Kumar V, Konar A, Hazra S. Intracameral use of nepafenac: safety and efficacy study. Current Eye Research. 2018 May 4;43(5):630-8.
12. 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):1089-93.
13. Sahu S, Ram J, Bansal R, Pandav SS, Gupta A. Effect of topical ketorolac 0.4%, nepafenac 0.1%, and bromfenac 0.09% on postoperative inflammation using laser flare photometry in patients having phacoemulsification. Journal of Cataract & Refractive Surgery. 2015 Oct 1;41(10):2043-8.
14. Kim SJ, Schoenberger SD, Thorne JE, Ehlers JP, Yeh S, Bakri SJ. Topical nonsteroidal anti-inflammatory drugs and cataract surgery: a report by the American

Academy of Ophthalmology. Ophthalmology. 2015 Nov 1;122(11):2159-68.

15. Duong HV, Westfield KC, Chalkley TH. Ketorolac tromethamine LS 0.4% versus nepafenac 0.1% in patients having cataract surgery: prospective randomized double-masked clinical trial. Journal of Cataract & Refractive Surgery. 2007 Nov 1;33(11):1925-9.
16. Toyos MM. Comparison of once-daily bromfenac 0.07% versus once-daily nepafenac 0.3% in patients undergoing phacoemulsification. Ophthalmology and Therapy. 2019 Jun;8(2):261-70.
17. Nardi M, Lobo C, Bereczki A, Cano J, Zagato E, Potts S, Sullins G, Notivol R. Analgesic and anti-inflammatory effectiveness of nepafenac 0.1% for cataract surgery. Clinical ophthalmology (Auckland, NZ). 2007 Dec;1(4):527.
18. Hovanesian J, Holland E. Tolerability and toxicity of topically applied nepafenac 0.3% compared with generic ketorolac 0.5%. Journal of Cataract & Refractive Surgery. 2019 Feb 1;45(2):174-80.
19. Lindstrom R, Kim T. Ocular permeation and inhibition of retinal inflammation: an examination of data and expert opinion on the clinical utility of nepafenac. Current medical research and opinion. 2006 Feb 1;22(2):397-404.
20. Jones BM, Neville MW. Nepafenac: an ophthalmic nonsteroidal antiinflammatory drug for pain after cataract surgery. Annals of Pharmacotherapy. 2013 Jun;47(6):892-6.
21. Kawahara A, Utsunomiya T, Kato Y, Takayanagi Y. Comparison of effect of nepafenac and diclofenac ophthalmic solutions on cornea, tear film, and ocular surface after cataract surgery: the results of a randomized trial. Clinical Ophthalmology (Auckland, NZ). 2016;10:385.
22. Hoffman RS, Braga-Mele R, Donaldson K, Emerick G, Henderson B, Kahook M, Mamalis N, Miller KM, Realini T, Shorstein NH, Stiverson RK. Cataract surgery and nonsteroidal antiinflammatory drugs. Journal of Cataract & Refractive Surgery. 2016 Sep 1;42(9):1368-79.
23. Ramakrishnan S, Baskaran P, Talwar B, Venkatesh R. Prospective, randomized study comparing the effect of 0.1% nepafenac and 0.4% ketorolac tromethamine on macular thickness in cataract surgery patients with low risk for cystoid macular edema. The Asia-Pacific Journal of Ophthalmology. 2015 Jul 1;4(4):216-20.
24. Zanetti FR, Fulco EA, Chaves FR, da Costa Pinto AP, Arieta CE, Lira RP. Effect of preoperative use of topical prednisolone acetate, ketorolac tromethamine, nepafenac and placebo, on the maintenance of intraoperative mydriasis during cataract surgery: a randomized trial. Indian journal of ophthalmology. 2012 Jul;60(4):277.
25. Sarkar S, Mondal KK, Roy SS, Gayen S, Ghosh A, De RR. Comparison of preoperative nepafenac (0.1%) and flurbiprofen (0.03%) eye drops in maintaining mydriasis during small incision cataract surgery in patients with senile cataract: A randomized, double-blind study. Indian journal of pharmacology. 2015 Sep;47(5):491.
26. Guzek JP, Holm M, Cotter JB, Cameron JA, Rademaker WJ, Wissinger DH, Tonjum AM, Sleeper LA. Risk factors for intraoperative complications in 1000

extracapsular cataract cases. Ophthalmology. 1987 May 1;94(5):461-6.
27. El Gharbawy SA, Darwish EA, Abu Eleinen KG, Osman MH. Efficacy of addition of nepafenac 0.1% to steroid eye drops in prevention of post-phaco macular edema in high-risk eyes. European Journal of Ophthalmology. 2019 Jul;29(4):453-7.
28. Danni R, Viljanen A, Aaronson A, Tuuminen R. Preoperative anti-inflammatory treatment of diabetic patients does not improve recovery from cataract surgery when postoperatively treated with a combination of prednisolone acetate and nepafenac. Acta ophthalmologica. 2019 Sep;97(6):589-95.