Study on the effect of topical Nepafenac 0.1% w/v in preventing Macular edema after cataract surgery in patients with diabetes

Ramalingam Kothai[1]*, Kalaimamani Ezhilvendhan[2], Iyyappan Saranya[1], Sivamurugan Rajesh Kanna[1] and Vijayan Roshini[1]

1. Department of Pharmacy Practice, Vinayaka Mission's College of Pharmacy, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, INDIA
2. Department of Ophthalmology, Vinayaka Mission's Kirupanandha Variyar Medical College and Hospitals, Vinayaka Mission's Research Foundation (Deemed to be University), Salem, Tamil Nadu, INDIA

*kothair@vmpha.edu.in; arul1971@gmail.com

Abstract

Cystoid macular edema (CME) is one of the major problems in diabetes patients after cataract surgery, which leads to fluid accumulation within the macular region. This clinical study aims to evaluate the effect of topical nepafenac 0.1% in preventing macular edema. The prospective interventional clinical study was conducted in the Department of Ophthalmology of a tertiary care hospital at Salem for a period of six months from Jan 2024 to June 2024. Investigations include random blood sugar (RBS), visual acuity, macular thickness and intraocular pressure (IOP) done on patients. 50 patients received sterile ophthalmic suspensions of 0.1% nepafenac and 50 patients received 0.5% carboxy methyl cellulose as placebo, both used thrice in a day before and after cataract surgery. Optical coherence tomography (OCT) was performed both pre-operatively before cataract surgery and up to 90 days after post-operative.

The outcome of this study shows a gradual decrease in macular thickness and, an increase in visual acuity. This study negotiates that nepafenac 0.1% was effective in preventing macular edema. It is considered to be safe and no complications were developed in patients subjected to nepafenac after cataract surgery in diabetes patients.

Keywords: Cystoid macular edema, Nepafenac, Macular thickness, Visual acuity, Optical coherence tomography.

Introduction

Cystoid macular edema (CME) is a common cause of poor visual outcomes after intraocular cataract surgery, which develops excess fluid accumulation within the macular retina[7,9]. The incidence of 20% of high volume of cataract surgeries is a common cause of poor vision that leads to CME[2]. The specific etiology of pseudophakic macular edema is not clearly understood[5], but CME is associated with the blood-retinal barrier disturbance induced by prostaglandins and other inflammatory mediators. CME occurs in a variety of clinical conditions such as diabetic retinopathy (DR), cataract phacoemulsification, retinal vein occlusion and intra-ocular inflammation. Many causes have been evaluated to contribute to its development such as light toxicity, cataract surgery, inflammatory mediators, vitero macular traction, age, vitreous loss, use of adrenergic drugs, hypertension (HTN) and diabetes mellitus (DM), iris incarceration[8]. The excess fluid accumulation within the macular retina develops CME. CME is distinguished as acute when it appears within 4 months after surgery, late-onset when it appears more than 4 months and chronic when it lasts over 6 months[6,10]. On the basis of diagnosing macular edema through OCT shows large intra–retinal Cystoid spaces with intervening septae. They are initially constricted to the outer retina mostly but gradually fuse to involve the entire thickness of the retina. The absence of exudates in the posterior pole and no (or) little diabetic retinopathy (DR) are suggestive of CME.

Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are used both pre-operatively and post-operatively to prevent or decrease inflammation after cataract surgery. NSAIDs block the COX enzymes, which are responsible for the production of prostaglandins and reduce the occurrence of pseudophakic cystoid macular edema (PCME) after cataract surgery[1]. Different types of NSAIDs have been preferred for the prevention and management of CME, including diclofenac, bromfenac, nepafenac, ketorolac tromethamine and flurbiprofen[13].

Nepafenac is approved by the Central Drugs Standard Control Organization (CDSCO) for the treatment of pain and inflammation correlated with cataract surgery and to diminish the risk of post-operative macular edema after cataract surgery in diabetic patients[4]. The drug nepafenac seems to be more progressive when compared to other NSAIDs in terms of ocular perforation allowing higher and sustained therapeutic levels in the retina and choroid. It crosses the cornea 6 times faster than diclofenac. Nepafenac is a prodrug that is deaminated to its active for Amfenac[6]. Nepafenac is available as 0.1% and 0.3% ophthalmic suspension[14]. The reason for the study is to describe the incidence of macular edema after phacoemulsification and intra-ocular lens implantation and to evaluate the efficacy of nepafenac in the prevention of macular edema after cataract surgery in diabetes patients.

Material and Methods

It was a prospective, interventional study on the effect of topical nepafenac 0.1% in preventing macular edema after

cataract surgery in patients with diabetes in a tertiary care hospital in Salem. The study was conducted by following the good clinical practices and the ethical principles characterized within the Declaration of Helsinki, during the duration of 6 months from Jan 2024 to June 2024 on the patients admitted to the Ophthalmology Department of the tertiary care hospital. The study proposal was submitted to the institutional committee and was approved (Tracking no: VMKVMC&H /IEC/24/082). The sample size was calculated by using the Solvins formula, 100 patients were involved in this study.

The written consent form was collected from all the patients involved in this study by the investigators prior to making them part of the study. Patients were assessed for safety and efficacy on the pre-operative day and post-operative days such as days 3, 14, 30, 45, 60 and 90. Patients were selected based on various criteria: patients of any ethnicity who were aged above 40, patients of both genders, patients with diabetes and patients who underwent cataract surgery. The exclusion criteria were the patients who have a history of previous ocular surgery, pre-existing histories of retinal vein occlusions, inflammatory eye diseases, ocular traumas, patients with glaucoma and uveitis, patients with DR and nephropathy, Ocular allergies to nepafenac and complications during cataract surgery like zonular dialysis, nucleus drop, vitreous loss posterior capsular rupture are found.

The ocular examination involves the best corrected visual acuity (BCVA), macular thickness and intraocular pressure. The BCVA was assessed by a certified optometrist by using a sellens chart. The visual acuity was converted into logarithm of the minimal angle of resolution (log MAR) chart values by using the formula:

$$\text{Log MAR} = \frac{Sellen\ Denominator}{Sellen\ Numerator}$$

Macular thickness was measured by using optical coherence tomography.

Data were collected from preoperative days and days 3, 14, 30, 45, 60 and 90 of post-operative cataract surgery. The patients were randomized into two groups. Group one received sterile ophthalmic suspension i.e. nepafenac 0.1% and group two received carboxy methyl cellulose as a placebo. The study focuses on finding the effect of topical nepafenac 0.1% in preventing macular edema after cataract surgery in patients with diabetes. The reason for the study was to describe the incidence of macular edema after phacoemulsification and intra-ocular lens (IOL) implantation and to evaluate the efficacy of nepafenac for up to 90 days after cataract surgery in the prevention of Macular edema and associated loss of visual acuity in diabetes patients. This clinical study aims to evaluate the effect of topical nepafenac 0.1% in preventing macular edema after cataract surgery in patients with DM, to find the post-operative visual outcome and to evaluate the post-operative macular edema.

Results and Discussion

In this study, hundred cataract surgery patients with diabetes were enrolled. The patients were randomly divided into two groups, one group received nepafenac 0.1% and another group received carboxyl methyl cellulose to evaluate their visual acuity and macular thickness. There were 54 males and 46 females respectively. Most of the patients were in the age range of 40-69 and fewer were in the range of 70 -89 involved in this study (Table 1).

Figure 1 shows the use of the drug nepafenac in the patients based on the duration of diabetes. The use of the drug is high between the duration of 1-10 years in diabetes patients. Patients were followed up on pre-operative and post-operative days such as days 3, 14, 30, 45, 60 and 90. The best corrected visual acuity was studied using snellens acuity chart converted to the logarithm of the minimal angle of resolution (log MAR) scale. The mean of log MAR BCVA was improved from Pre-OP (0.78) to day 90 (0.15). This shows a significant increase in the visual acuity. BCVA was improved when compared to the pre-op VA to day 90 VA (Figure 2).

In the analysis of mean macular thickness by using OCT, the mean value of Pre-OP macular thickness with the drug nepafenac is 219.75 and the day 90 MT was 252.83 and the mean of the carboxyl methyl cellulose (placebo) is 222.76 and the day 90 MT was 268.83. This shows that the use of nepafenac decreases the macular thickness when compared to carboxyl methyl cellulose. (Table 2).

Table 1
Analysis of the cases studied according to demographic details

Demographic data		No. of. People
Gender	Male	54
	Female	46
Age (years)	40-49	27
	50-59	25
	60-69	28
	70-79	19
	80-89	1

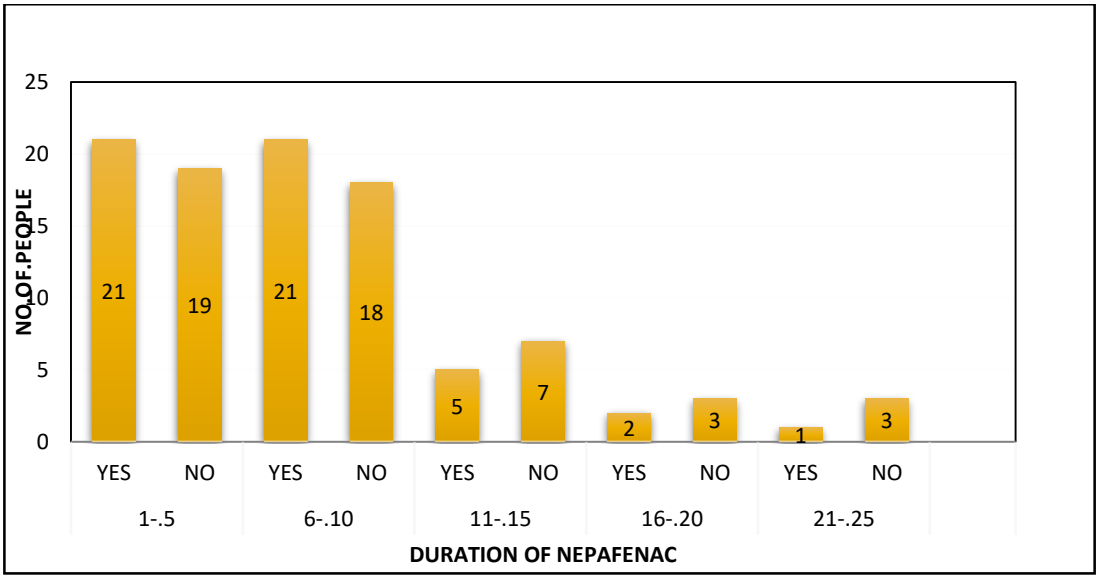

Figure 1: Analysis of the drug use based on the duration of diabetes

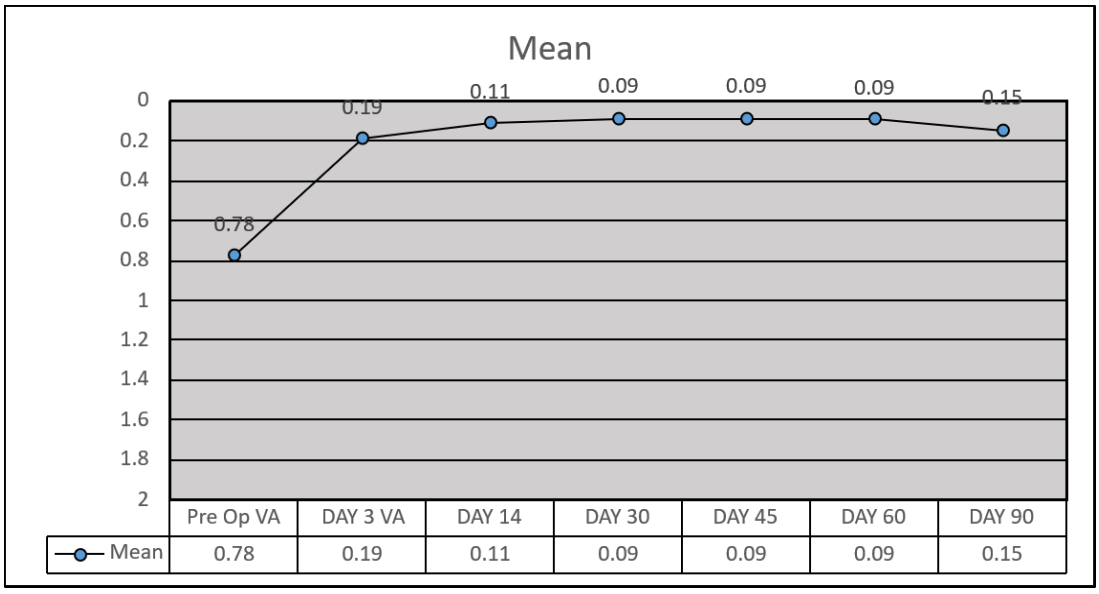

Figure 2: Visual acuity assessment based on Log MAR – Mean improvement

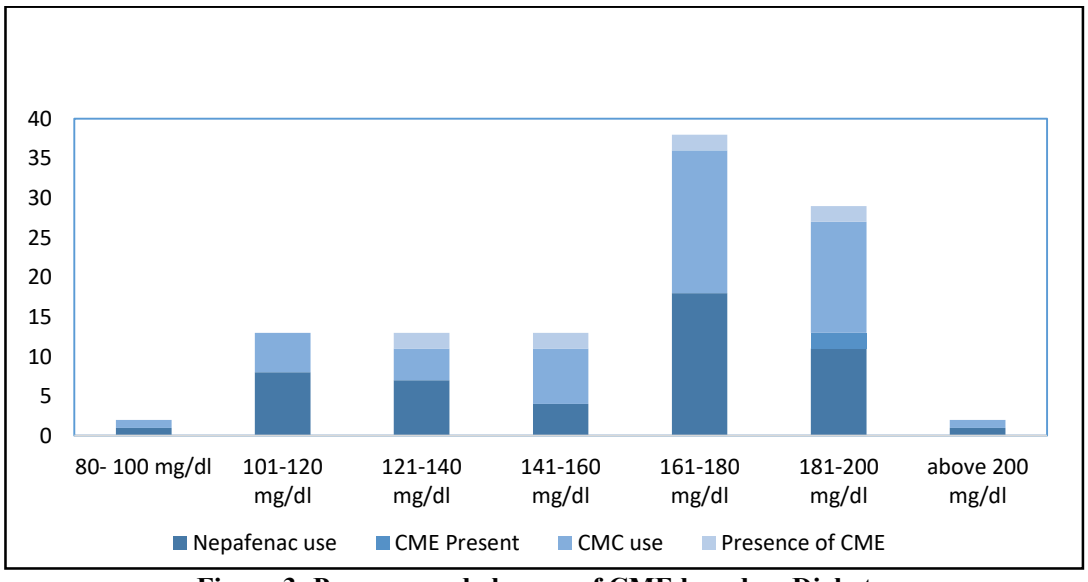

Figure 3: Presence and absence of CME based on Diabetes

Table 2
Analysis of studied eyes according to the macular thickness (µ)

Treatment	Pre-op MT	Day 3MT	Day 14MT	Day 30MT	Day 45MT	Day 60MT	Day 90MT
Nepafenac	219.75 ±32.95	234.60± 35.12	238.79± 34.91	243.28± 34.72	245.68± 35.36	249.66± 37.81	252.83± 43.51
Carboxy methyl cellulose	222.76± 32.71	237.85 ±32.09	246.06 ±33.68	255.12 ±43.62	259.80 ±47.91	266.47 ±53.62	268.00 ±55.88

The analysis of RBS was done to find the presence and absence of CME based on the administration of Nepafenac and CMC. After the use of nepafenac, 2 % of people developed CME in the RBS range of 181-200 mg/dl and in the use of CMC, 8% of people developed CME in the RBS range of 121-140 mg/dl,141-160 mg/dl,161-180 mg/dl,181-200 mg/dl.

Collectively, this study shows the decrease in the macular thickness by OCT and improved visual functions by BCVA after the dose of nepafenac drug from Pre-OP to day 90 (Figure 3). The prospective clinical study signifies that based on vision and retinal thickness, treatment with the onset of nepafenac pre-surgically and used up to 90 days after cataract extraction was related to a depletion in risk of macular edema corresponding with a decrease of visual acuity in diabetes patients. In this clinical study, few people have developed macular edema in the nepafenac 0.1% group compared to carboxy methyl cellulose. This clinical study was conducted in diabetic patients since it is clearly established that changes in the macular region are more likely to occur after cataract surgery in following patients[13].

This clinical study demonstrates that the pre-operative visual acuity is 0.78, after the post-operative cataract surgery with the treatment of nepafenac 0.1 % the visual acuity improved to 0.15. The macular thickness is also reduced after the use of nepafenac 0.1%. In this clinical study OCT is regarded as a well-found method for establishing the diagnosis of postsurgical CME because it shows the typical morphological modifications in the macula, including the well-defined cysts in the outer plexiform layer. Fluorescein angiography was not used to detect Irvine Gass syndrome[11].

Many ways have been characterized for the treatment of postoperative cystoid macular edema. Following cataract extraction, eyedrops containing steroids and NSAIDs are administered either alone or in combination to treat macular edema. In clinical practice, steroids have also been used as intravitreal or peribulbar injections but steroids are known to increase the intraocular pressure in a percentage of patients. Oral carbonic anhydrase inhibitors are considered the second-line treatment. NSAIDs are the most commonly used treatment for macular edema after cataract phacoemulsification. Nepafenac is the first prodrug in NSAID formulation and it is an ophthalmic suspension that plays a major role in the treatment of pain and inflammation associated with cataract surgery. It is COX1 and COX2 inhibitor[12]. Nepafenac enters the cornea quickly and is broken down by intraocular hydrolases in the retina, choroid and ciliary body epithelium to produce the active metabolite, amfenac. Amfenac and nepafenac are strong inhibitors of the isoforms of the Cox enzyme. In the vascularized tissues of the eye, nepafenac exhibits long-term action. It is used to treat post-cataract surgical symptoms such as eye edema, redness, pain etc. Nepafenac appears superior to other NSAIDs in the matter of ocular penetration and higher and sustained therapeutic levels in the retina and choroid.

The patients did not report any significant ocular adverse effects during the follow-up, despite the fact that topical NSAIDs have been known to cause corneal epithelium damage, epithelial abnormalities and even corneal melting. However, ongoing monitoring and follow-up of these patients are still required because the data about long-term NSAID use is still insufficient[1]. The effect of nepafenac 0.1% in preventing macular edema by increasing the visual acuity reducing the macular thickness and preventing vision loss has been shown in several studies[3,14]

Conclusion

From this study, it may be concluded that the drug nepafenac was found to be effective in the prevention of macular edema. It is considered to be safe and no complications were developed in patients subjected to nepafenac following cataract surgery in diabetes patients. The use of nepafenac is recommended for at least three months after cataract surgery.

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