

EVALUATION OF MACULAR THICKNESS IN DIABETIC MACULAR EDEMA TREATED WITH 0.1% NEPAFENAC WITH CONTROL AND UNCONTROLLED GLYCEMIC LEVEL

¹Sana Maqsood, ²Tehreem Maqsood, ³Mehroz Shahid, ⁴Adila Qasim, ⁵Ammara

ABSTRACT

Objective: To evaluate the effect of 0.1% Nepafenac on macular thickness and visual acuity in diabetic macular edema with controlled and uncontrolled glycemic controls.

Methodology: A Quasi experimental study design was used. This study included 60 patients with age above 15 years. Data was collected at the Department of Ophthalmology in Madina Teaching Hospital Faisalabad. 30 participants with controlled sugar levels were in group 1 remaining 30 participants with uncontrolled blood sugar were in group 2. Both groups were treated with 0.1% Nepafenac eye drops. Visual acuity and macular thickness was evaluated before and after treatment with the help of questionnaire. Participants were for follow up at 4th and 6th week. Statistical analysis was done by using repeated measure ANOVA and Independent sample t-test.

Results: The mean value of macular thickness at baseline was 441.6667 in controlled sugar groups while 518.4000 in uncontrolled after 4 weeks of using nepafenac was 433.7000 in control sugar group and 516.0333 in uncontrolled and after 6 weeks was 425.7667 and 512.4667 in control and uncontrolled sugar level groups respectively and p value was (p= .000). The mean of visual acuity at baseline was .7533 and .8367 while after 4 weeks was .7533 and .8367 while after six weeks was .6000 and .7000 in control and uncontrolled respectively. P value for visual acuity at baseline, after 4 and six weeks was .024, .024 and .0234 respectively in control and uncontrolled sugar groups.

Conclusion: Topical nepafenac is effective in improving macular thickness and vision in accordance with different blood sugar levels. Topical nepafenac works more efficiently if patient has controlled blood sugar level.

Keywords: Nepafenac, Visual Acuity, Macular Thickness

INTRODUCTION

Diabetes is a group of systemic disorders mostly affecting the tiny vessels of the body in which there is a defect in insulin production or in working of insulin results in higher blood glucose levels abnormally. Insulin is a metabolic hormone. Disturbance in insulin working results in malformation of other macromolecules necessary for proper functioning of human body. The progression and sternness of systemic disease and its treatment succession rate depends upon controlled and uncontrolled blood sugar level (1).

Main troublesome thing about diabetes is diabetic retinopathy which itself is a huge cause of vision loss in common people. Due to prolong diabetes many changes occur in retina known as diabetic retinopathy. Diabetic retinopathy is the prime origin of blindness. It can occur at any age. It depends on blood sugar levels and period of diabetes. It has four stages. Full detailed fundus examination is required. Not only retina many other parts of eyes get affected by diabetes including cornea and anterior segments. Proper management of blood sugar level is required to minimize the consequences of diabetes (2). Gradual gathering of fluid present inside the retina between different layers of retina results in increase width of retina due to diabetic retinopathy known as diabetic macular edema. Blood vessels in the retina has no apertures and compact bond are present between the cells so no chances of blood leakage inside the retina under normal conditions (3). Prolonged increased blood glucose level affects the normal structures of blood vessels inside the retina results in the leaky blood vessels. Advancement of diabetic macular edema hangs on the degree of blood glycemic levels and on the period of diabetes (4). Two types of macular edema clinically significant and clinically non-significant. Increased thickness of retina at macula centre or rigid oozes are present at five hundred microns meter of macula centre with increased retinal thickness or increased retinal thickness of 1 disc region either in the disc region of macula centre or at some piece of retina.

Corresponding author: Sana Maqsood

^{1,2,3,4,5} School of Optometry, The University of Faisalabad

If any one of the above finding is seen upon optical coherence tomography is considered as clinically significant macular edema. In clinically non significant edema small increase in macular thickness is seen upon optical coherence tomography (5). In whole world more than four hundred million people were suffering from diabetes. According to the recent surveys researchers estimated that number of diabetic persons may reached to six hundred and fifty millions after twenty years. As the number of diabetic patients increase rate of complications associated to it also increased. Until now diabetic retinopathy which was a complication of uncontrolled diabetes is considered as major cause of vision loss in people around the globe. Patients having type 2 diabetes are at higher risk to develop macular edema. Diabetic macular edema itself is a big cause of avoidable blindness with 6.8 percent prevalence around the world. Worldwide twenty seven million people were suffering from diabetic macular edema due to uncontrolled diabetes for a longer period of time (6).

Many treatment options are available in the market for the diabetic macular edema. Grid and focal lasers are two types of laser therapy used for treating macular edema due to diabetic retinopathy. Commonly used vascular endothelial growth factor inhibitor includes bvacizumab, ranibizumab and pegaptanib sodium. Dexamethasone, triamcinolone and fluocinolone are commonly used intra vitreal steroids for treating macular edema. Surgical option to treat macular edema due to diabetes is the removal of vitreous. Non-steroidal anti-inflammatory drugs are another option available for treatment with lesser chances of treatment consequences (7).

Topical 0.1% nepafenac is a favorable cure for treating macular edemas and improving vision in patients with macular edemas (8). The objectives of this research study was to evaluate the effect of 0.1% Nepafenac on macular thickness in diabetic macular edema with controlled and uncontrolled glycemic controls. To evaluate the effect of 0.1% Nepafenac on visual acuity in diabetic macular edema with controlled and uncontrolled glycemic levels.

MATERIALS AND METHODS

A Qusai Experimental study design was used. Study was conducted at Department of Ophthalmology in Medina Teaching Hospital Faisalabad. Study was conducted from September 2021 to June 2022. Non probability Purposive sampling was used. 60 patients were included. Males and females both genders were included. Age ranges from 15 year onward was included. Diabetic macula edema treated with 0.1% Nepafenac was included. Patient's with controlled glycemic levels were included. Patients with uncontrolled glycemic levels were included.

Patients with advance stage of diabetic retinopathy were excluded. Patient treated with vascular endothelial growth factor inhibitor and laser therapy excluded. Log MAR (Haag Striet, UK) acuity chart was used for measuring visual acuity. OCT (Niddek RS 3000) was performed to kept the record of macular thickness. 0.1% Nepafenac eye drops was used. HbA1c test was used to evaluate blood sugar levels. Self design profroma was used for evaluation.

Basic ocular examination includes demographic data, history and visual acuity of every patient was checked by Log MAR chart. Macular thickness of every patient was evaluated by ocular coherence tomography at first visit, four and six week's visits. All patients included in this study were divided into groups. Thirty patients were kept in each group. In group one I kept the patients who were having the controlled blood sugar levels. In group two patients having the uncontrolled blood sugar levels were placed. Before the start of the study and at the end of this study HbA1c was performed to kept the record of blood sugar level of all the patients taking part in this study. Topical 0.1% Nepafenac drops were given to all patients to use 3 times a day. Patients were asked for follow up at 4th week and 6th week of using topical 0.1% topical nepafenac.

HbA1c test gives us previous 3 months record of the patients blood sugar level. According to the HbA1c test if patient has HbA1c level less than 7.0% it is considered as controlled blood sugar level and in poorly controlled diabetes its level is 8.0% or above. Log MAR chart is used to assess a patient's visual acuity. Log MAR chart is performed at 4m distance. Occlude the non- testing eye of the patient. Ask the patient to read the first letter of the chart. Every letter of log MAR chart has 0.02 log value. There are 5 letters in one line of log MAR chart. One line of log MAR chart has a change of 0.1 log units. Note down the lines and letters read by the patients without difficulty. For recording the visual acuity through this chart unseen letters are added on the same line. If the patient finds the difficulty in reading the first letter of the chart reduce the distance of the chart from 4 to 2 meters still patient find difficulty in reading reduce the distance to 1m. Note down the line and letters read by the patient. If patient read the two letters of 0.9 line at 2 meters distance visual acuity of the patient is $0.3+0.02+0.02+0.02+0.9 = 1.26$. Add 0.3 every time you reduce the distance of the chart. The normal range of log MAR chart is 1.00 to 0.00. If patient has read the 0.30 line marked on chart it means his visual acuity is good as compared to the patient reading the 0.70 line on the chart.

Optical coherence tomography (OCT) is a non-invasive technique which is use in assessing the different layers present at the back of the eye up to the optic nerve. Light waves are used in optical coherence tomography machine

for the assessment of the retina. Light waves used in OCT are not harmful to the human eye. In this research macular thickness of all the patients was assessed using the optical coherence tomography. Vitreous diseases, changes in macula and changes in the optic nerve can also be detected by using OCT. Explain the whole procedure to the patient to make the patient comfortable. Ask the patient to sit on the chair and place his head in the head rest of OCT machine. Enter the data of the patient in the machine. Focus the part of the retina you want to observe. Three dimensional images of the retina are obtained by using OCT. Patient compliance is good in this procedure as this technique is non-contact. Normal average value of macular thickness is from 212 microns meter to 230 microns meter. Macular thickness of each patient is recorded and compared to the normal value. Data analysis was done on SPSS by applying repeated measure ANOVA and Independent Sample t-test.

RESULTS

Out of sixty patients, thirty patients were kept in controlled and thirty in uncontrolled sugar group. Out of the total sixty subjects for this study, 56.7% (N=34) were males and 43.3% (N=26) were females.

Table 1: Assessment of Macular thickness in control sugar group levels in diabetic macular edema using nepafenac

	Mean	St. Deviation	N	Sig
Data of macular thickness before using nepafenac in controlled sugar group	441.6667	13.56297	30	.000
Data of macular thickness after four weeks of using nepafenac	433.7000	11.03646	30	
Data of macular thickness after six weeks of using nepafenac	425.7667	10.55260	30	

St. Deviation: Standard Deviation , N: Sample size, Sig: Significance

Table 2: Assessment of visual acuity with control sugar levels in diabetic macular edema using nepafenac

	Mean	St. Deviation	N	Sig
Data of visual acuity before using nepafenac in controlled sugar group	.7533	.15477	30	.000

Data of visual acuity after four weeks of using nepafenac	.7533	.15477	30	
Data of visual acuity after six weeks of using nepafenac	.6000	.15313	30	

Table 3: Assessment of macular thickness in uncontrolled sugar level group in diabetic macular edema using nepafenac

	Mean	St. Deviation	N	Sig
Data of macular thickness before using nepafenac in uncontrolled sugar group	518.4000	46.71085	30	.000
Data of macular thickness after four weeks of using nepafenac in uncontrolled group	516.0333	46.23813	30	
Data of macular thickness after six weeks of using nepafenac in uncontrolled group	512.4667	46.54011	30	

Table 4: Assessment of visual acuity in uncontrolled sugar levels in diabetic macular edema using Nepafenac

	Mean	St. Deviation	N	Sig
Data of visual acuity before using nepafenac in uncontrolled sugar group	.8367	.12172	30	.000
Data of visual acuity after four weeks of using nepafenac	.8367	.12172	30	
Data of visual acuity after six weeks of using nepafenac	.7000	.11744	30	

The p value for macular thickness obtained from Independent sample t test was ($p = .000$) after 4 and 6 weeks of using nepafenac drops between control and uncontrolled group patients indicating that significant difference was present between both the groups. The p value for visual acuity after 4 and six weeks of using nepafenac was ($p = .024$) and ($P = .006$) between control and uncontrolled sugar groups indicating that significant improvement in visual acuity was seen between both groups.

DISCUSSION

Nepafenac eye drops works with more efficiency if patient's blood sugar level is controlled. Topical Nepafenac is another available option for treating diabetic macular edema. Nepafenac eye drops can perforate through vitreous therefore they are now considered as a good option for treating redness in eye, eye inflammations and macular edemas due to diabetes (9). Nepafenac has greater penetrability through cornea and becomes active as soon as entered in body. Nepafenac is a strong constraint of cyclooxygenase enzyme which is very important for inflammatory response. Nepafenac reduce the inflammatory response (10). Nepafenac has become a drug of choice for treating macular edemas. All ophthalmologist prescribed nepafenac as it provides better results with lesser

treatment consequences. Nepafenac has some side effects like itching in the eyes, headache, nausea and vomiting. Nepafenac eye drops cannot use for longer duration of time. Doctors have to monitor the patients continuously using nepafenac eye drops. In 2019 Mridula Amarnath performed a research to find out efficacy of nepafenac eye drops in treating macular edema. 14 eyes were included in this study. According to the results of this research study the mean value of visual acuity at second, fourth and sixth month was 0.34, 0.25 and 0.18 respectively. P value was $p = 0.025$ indicating that significant improvement was seen in the visual acuity after using nepafenac for six months. It is concluded that topical nepafenac was a cheap and protective drug in treating diabetic macular edema (11) while in the present study mean value of visual acuity in control sugar group was .7533 at base line, was .7533 after four weeks of using and was .6000 after six weeks of using while was .8367, .8367 and .7000 at baseline, after four weeks and six weeks of using nepafenac respectively in uncontrolled sugar level group showing that visible difference was present in visual acuities of both groups. The P value was ($p = .024$) which was < 0.05 indicating that nepafenac could be used for improving vision in all diabetic macular edema patients. It was concluded that topical nepafenac was found very effective in reducing macular thickness in accordance with different blood sugar levels. It was concluded that nepafenac eye drops were found effective in improving vision in both controlled and uncontrolled sugar level groups. Topical nepafenac 0.1% works more efficiently if patient has controlled blood sugar level. It is necessary to advise the patient to take diabetic medications as prescribed by the physician so that drug could work more efficiently. After many researches done on Nepafenac eye drops it is found that it can also be used to treat post operative pain and redness. Nepafenac eye drops are found very effective in preventing macular edema after removal of crystalline lens. The limitations of this study are Difficulty in collecting the data at follow ups as patient hardly came for follow ups. Patients hardly use same drug for six weeks continuously. Difficulty in keeping record of patients blood sugar level on daily basis. HbA1c is a costly test every patient cannot afford that limits participation of patients in this research study. Nepafenac is a cheap and productive drug available in the market for treating diabetic macular edema. Eye doctors should prescribed nepafenac 0.1% instead of costly treatment option available in the market. More research should be done on nepafenac working in reducing swelling and pain after intra ocular lens removal.

References

- (1). Kharroubi AT, Darwish HM. Diabetes mellitus: The epidemic of the century. *World journal of diabetes*. 2015 Jun 6; 6(60): 850.
- (2). Sabanayagam C, Banu R, Chee ML, Lee R, Wang YX, Tan G, Jonas JB, Lamoureux EL, Cheng CY, Klein BE, Mitchell P. Incidence and progression of diabetic retinopathy: a systematic review. *The lancet Diabetes & endocrinology*. 2019 Feb 1;7(2): 140-9.
- (3). Hariprasad SM, Callanan D, Gainey S, He YG, Warren K. Cystoid and diabetic macular edema treated with nepafenac 0.1%. *Journal of Ocular Pharmacology and Therapeutics*. 2007 Dec 1; 23(6): 585-90.
- (4). Bowling B. *Retinal Vascular Diseases*. Kanski's Clinical Ophthalmology. 2019. Eighth edition. 633-635.
- (5). Jogi R. *The Retina*. Basic Ophthalmology. 2017. Fifth edition. 348-357.
- (6). Bursell SE, Fonda SJ, Lewis DG, Horton MB. Prevalence of diabetic retinopathy and diabetic macular edema in a primary care-based teleophthalmology program for American Indians and Alaskan Natives. *PLoS One*. 2018 Jun; 20; 13(6): 198-551.
- (7). Udaondo P, Adan A, Arias-Barquet L, Ascaso FJ, Cabrera-López F, CastroNavarro V, Donate-López J, García-Layana A, Lavid FJ, Rodríguez-Maqueda M, Ruiz-Moreno JM. Challenges in diabetic macular edema management: an expert consensus report. *Clinical Ophthalmology*. 2021 July; 15: 3183-3195.
- (8). Aaronson A, Achiron A, Tuuminen R. Clinical course of pseudophakic cystoid macular edema treated with nepafenac. *Journal of clinical medicine*. 2020 Sep 21; 9(9): 3034.
- (9). Gundogan FC, Yolcu U, Akay F, Ilhan A, Ozge G, Uzun S. Diabetic macular edema. *Pakistan journal of medical sciences*. 2016 Mar; 32(2): 505.
- (10). Riccardo S, Chiara G, Eleonora C, Enrico B, Giuseppe Q, Francesco B. Emerging therapies in the management of macular edema: a review. 2019; 8.
- (11). Amarnath MV. Efficacy of topical nepafenac in treatment of diabetic macular edema. *International Journal of Pharmacognosy*. 2019 Dec; 6(12): 407-410.