

## ORIGINAL ARTICLE

# Topical Sodium Diclofenac during Pan-Retinal Photocoagulation in Patients with Proliferative Diabetic Retinopathy

ABDUL AZIZ<sup>1</sup>, ZUBAIRULLAH KHAN<sup>2</sup>, MUHAMMAD AYUB KHAN<sup>3</sup>, SALAHUDDIN<sup>1</sup>, AFRASIAB<sup>4</sup>, MARIAM ZAKIA CHAUDHARI<sup>5</sup>

<sup>1</sup>Resident Medical Officer Ophthalmology, Hayatabad Medical Complex, Peshawar

<sup>2</sup>Assistant Professor Ophthalmology, Woman Medical and Dental College, Abbottabad

<sup>3</sup>Assistant Professor Ophthalmology, Gomal Medical College, Dera Ismail Khan

<sup>4</sup>Medical Officer Ophthalmology, DHQ hospital, LakkimMarwat

<sup>5</sup>Assistant Professor Ophthalmology, Amna Inayat Medical College/ Kishwar Fazal Teaching hospital, Lahore

Corresponding author: Zubairullah Khan, Email: [zubairw78@gmail.com](mailto:zubairw78@gmail.com), Cell: +92 346 9749049

## ABSTRACT

**Aim:** To determine the 0.1 percent topical sodium diclofenac analgesic effect on the retina during laser photocoagulation.

**Study Design:** Arandomized prospective control study.

**Place and Duration:** In the Ophthalmology department of Hayatabad Medical complex Peshawar and Woman Medical and Dental College, Abbottabad for duration of six months from November 2020 to April 2021.

**Methods:** The study included 90 people with 47 cases of proliferative diabetic retinopathy who had two sessions of pan-retinal photocoagulation (group A) as well as 43 people with non-proliferative diabetic retinopathy who received bilateral grid treatment (group B) (group B).sodium chloride 0.9% or Sodium diclofenac 0.1% topical drops were instilled 30–135 mints formerly to treatment with laser in a concealed fashion. When a patient had 2 sessions, the alternative medicine was administered in the second session. The visual analogue scale was castoff to measure the amount of pain immediately after the laser therapy (VAS). The findings were subjected to statistical analysis

**Results:** In 84/90 sessions, patients in A grouptestifiedpain (93.3 percent). When 0.1 percent sodium diclofenac drops were instilled, the mean stated grade of pain was 47.8 percent, and when 0.9 percent sodium chloride drops were instilled, the mean reported degree of pain was 53.3 percent. Only 14/60 sessions (23.3 percent) of patients in group B reported pain, and pain levels varied from 10% to 60% depending on the kind of drops administered. There was no link between pain intensity and the time it took to go from applying the drops to laser therapy (30–135 minutes) or the average energy level utilized (100–500 mW) in either group.

**Conclusion:** Pan-retinal photocoagulation should be performed after the administration of sodium diclofenac 0.1 percent, which is an excellent pain reliever.

## INTRODUCTION

Non-steroidal anti-inflammatory medications are a class of pharmaceuticals that are used as analgesics, antipyretics, and anti-inflammatory agents either systemically or locally<sup>1-2</sup>. The phenyl acetic acid chemical family includes sodium diclofenac 0.1 percent (VoltarenOphtha), which is commonly used as pain-relieving for the anterior region of the eye<sup>3-4</sup>. It has been demonstrated to reduce corneal sensitivity in human cornea and to have a high effect in corneal abrasion patients<sup>5</sup>. It also helps to alleviate discomfort during cataract surgery, radial keratectomy, & excimer photorefractive keratectomy, among another procedures<sup>6-7</sup>. Sodium diclofenac 0.1 percent was shown to be effective in individuals undergoing scleral buckling and vitrectomy in one trial evaluating its use in the posterior region<sup>8-9</sup>. Within the focus of this research, the analgesic impact of sodium diclofenac 0.1 percent drops in the context of retinal laser treatment was studied.

## PATIENTS AND METHODS

The randomized prospective control study was held in the Ophthalmology department of Hayatabad Medical complex Peshawar and Woman Medical and Dental College, Abbottabad for duration of six months from November 2020 to April 2021. Study participants consisted of 90 patients, 47 with PDR (group A) and 43 with NPDRwith clinically

evident edema of the macula (group B). No prior laser therapy for any of the patients. A total of two laser treatments (90 sessions) were given to all patients in A group; in B group, one session laser treatment was given to 25 patients unilaterally andbilaterallyone session laser treatment was given to 18 patients. Each of the 40subjects in A group and 18 patients in B group received 100 mg salicylic acid daily.Both the sodium diclofenac 0.1 percent solution and the sodium chloride 0.9 percent solution were stored in thiomersal 0.04 mg and put in the same container, with the bottles labelled 1 and 2 were masked, respectively. Everysubject received one vial of drops from a table, which was chosen at random by the first researcher just before the first laser session began. Those patients who received drops from 1<sup>st</sup> bottle (0.1 percent sodium diclofenac) during the first laser session were managed with drops from bottle 2 (0.9 percent sodium chloride) following drops from bottle 1 (i.e., all of group A patients) during the second laser session. There is no odour and no discomfort associated with the use of sodium chloride and sodium diclofenac at small doses. For pupil dilation, drops of 0.5 percent tropicamide and 10% phenylephrine hydrochloride were employed. A single drop of benoxinate hydrochloride 0.4 percent was used as a local anesthetic right before the laser treatment was performed. Throughout the surgery, there was no anesthetic injection administered to the

patient. Another researcher (who used a contact lens to provide the laser therapy) was completely ignorant of the existence of the drops in the solution. A YAG laser with a 532 nm double frequency and 200 m spot size, 0.1 ms of exposure time, and 100–500 mW energy level was used by the researchers; the shot number fluctuated from 20 to 1000. The second researcher employed laser treatment between 30 and 135 minutes after administering the analgesic medicine to the subjects.

The 3<sup>rd</sup> investigator, who was too blind to the drops, used Scott's visual analogue scale to rate how much pain he felt right after the treatment, and he did the same thing (VAS).

The VAS is a ten-centimeter scale that changes from light to dark grey. White means no hurt or ache, and dark grey means the most pain you can imagine. 0 percent means no pain and 100 percent means a lot of pain. The percentages are based on the answers the people gave on the scale (worst pain).

Only at the conclusion of the research were all of the data masked and analyzed. We looked at two primary effects; individual pain ratings were compared after the first and second sessions with the alternative therapies in order to assess the overall painkilling effect of 0.1 percent sodium diclofenac during laser photocoagulation. The posterior pole laser treatment was compared to peripheral laser therapy in terms of the session number during which patients in groups A and B were uncomfortable. Furthermore, the number of laser treatments, the degree of energy used, and the time interval between analgesia and laser therapy were all investigated.

**Statistical analysis:** The statistical analysis used parametric tests (paired t and t), nonparametric testing (Mann–Whitney and Wilcoxon), correlation and Pearson's 2 tests. When a significant number of patients are involved, statistical parametric tests are frequently utilized. When we looked at the findings of the full group in our series, we applied this test. When the group was segregated by sex, the non-parametric test was applied. The association between factors such as the total laser shots, pain score and energy level was determined using Pearson's 2 and correlation tests.

**RESULTS**

The laser applications number, energy levels employed, and duration from analgesia or placebo to laser therapy (Table 1) were not substantially different between groups A and B.

Regardless of the analgesic medication utilized, individuals in group A testified no pain in just 6 of the 90 laser sessions (6.7%). Pain was noted in every single one of the remaining 84 sessions. When 0.1 percent sodium diclofenac drops were instilled, the mean stated grade of pain was 47.8 percent, and when 0.9 percent sodium chloride drops were instilled, the mean reported degree of pain was 53.3 percent. Because of this difference, a paired t test indicated that the p-value was significantly < 1 (p=0.01). The only difference between those who used sodium chloride and sodium diclofenac was that 10 out of 47 patients experienced higher pain while using sodium diclofenac; 8 patients reported no difference in pain. With

0.1 percent sodium diclofenac decreases (p = 0.0587 by Mann–Whitney test), men had 54.4 percent pain and females had 38.9 percent pain, while with 0.9 percent sodium chloride drops (p = 0.320 by Mann–Whitney test), males had 55.6 percent pain and females had 51.1 percent pain. Females experienced a significant difference (p = 0.0438 by Wilcoxon test) in pain levels reported with 0.1 percent sodium diclofenac vs 0.9 percent sodium chloride, whereas males did not (p = 0.1023 by Wilcoxon test). Salicylic acid was not associated with the severity of pain, the average energy level, or the time between treatments.

In group B, 46 of the 60 laser treatments resulted in no pain (76.7 percent). The intensity of pain varied from 10% to 60% in the remaining 14 sessions (23.3%), independent of the kind of drops utilized. There was a statistically significant difference in the number of sessions related with pain among A and B groups (p = 0.000 using the Pearson's 2 test) (Table 2).

Table 1: shows average treatment parameters

Group	Application	Energy	Time
(A) proliferative diabetic retinopathy			
0.1% Sodium diclofenac drops	550.1	319.7	67
0.9% NaCl drops	560.8	331.1	69.1
(B) non-proliferative diabetic retinopathy			
0.1% Sodium diclofenac drops	145.8	249.9	71.2
0.9% NaCl drops	132.1	271.1	70.9
p Value	0.46	0.62	0.8

Table 2: shows the pain levels linked with laser treatments to the peripheral and posterior poles

Groups	No pain	pain
NPDR Posterior pole treatment (B)	46	14
PDR PERIPHERAL treatment (A)	6	84
P value		0.000

**DISCUSSION**

NSAID sodium diclofenac was tested as an analgesic during retinal laser photocoagulation. The suppression of the arachidonic acid cascade is thought to be the fundamental mechanism for NSAIDs' analgesic effect<sup>9-10</sup>. The arachidonic acid cascade is divided into two halves by the enzyme's cyclooxygenase and lipoxygenase. In the cyclooxygenase system, the principal products are prostaglandins, Miosis, changes in intraocular pressure and augmented vascular permeability of blood-ocular barriers are some of the consequences of these agents, which also include additional side effects<sup>11-12</sup>. Prostaglandins also have chemokinetic action, which helps to sustain and enhance the humoral and cellular stages of the inflammatory response, when numerous mediators are produced that activate pain-producing nerve fibers. The lipo-oxygenase pathway produces leukotrienes as a byproduct<sup>13-14</sup>. Chemotaxis, chemokines is, plasma exudation, and phospholipase stimulation are all documented side effects<sup>15</sup>.

Indomethacin, which is a member of the indole

chemical family and was the first topical nonsteroidal anti-inflammatory drug (NSAID) to be used in ophthalmology, works by decreasing prostaglandin E2 levels in the human cornea, which is where the medicine is found in the highest concentrations<sup>16-17</sup>. In addition to its effect on the arachidonic acid cascade, sodium diclofenac 0.1 percent also has an effect on the lipoxygenase pathway at higher doses, which makes it an excellent anti-inflammatory agent. 12 The medication quickly enters the cornea and aqueous when administered topically<sup>18</sup>. At 2.4 hours after instillation, the maximum average concentration of the medication observed in the aqueous humour was 82 ng/ml. Topical sodium diclofenac works by causing aqueous to leak into the vitreous or by "desensitizing" the sensory fibers along the entire distribution of trigeminal nerves<sup>19</sup>.

We employed the VAS, which has been proved to be correlated and repeatable, in this study since pain feeling is subjective and its measurement is similarly subjective. The study's main conclusion was that patients given PRP pretreated with 0.1 percent sodium diclofenac drops had considerably lower self-reported pain levels than those pretreatment with 0.9 percent sodium chloride drops. Regardless of the fact that 10 of 47 patients had greater pain with diclofenac than sodium chloride, and 8 had identical pain levels with both treatments, the 30 patients who had less pain with diclofenac exceeded the nine who had more with sodium chloride. Although some individuals reported modest levels of discomfort and others severe levels, when sodium diclofenac was administered, the feeling was typically reduced. We found that the number of drops administered (20–1000), the laser energy level (100–500 mW), and the interval between drops and laser treatment (30–135 minutes) did not change the pain threshold. This was factual for the complete cohort as well as the different groups received treatment<sup>20-21</sup>.

Also, posterior pole treatment is related with no, moderate, or mild pain, which is clinically acknowledged but not statistically verified. The absenteeism of ache is probably owing to decreased power grid photocoagulation<sup>22-23</sup>. Acute macular photocoagulation with diclofenac employed an average power per pulse of 253 mW, whereas peripheral photocoagulation used average powers of 322–328 mW and 326 mW.

## CONCLUSION

In conclusion, it is suggested that sodium diclofenac 0.1 percent relieves pain more effectively than sodium chloride, suggesting that it is an effective analgesic and should be considered for PRP. Also, clinicians should be aware that treatments involving the peripheral segments are more unpleasant than posterior segment procedures.

## REFERENCES

1. Nikkiah H, Ghazi H, Razzaghi MR, Karimi S, Ramezani A, Soheilian M. Extended targeted retinal photocoagulation versus conventional pan-retinal photocoagulation for proliferative diabetic retinopathy in a randomized clinical trial. *International Ophthalmology*. 2018 Feb;38(1):313-21.
2. Sameen M, Khan MS, Mukhtar A, Yaqub MA, Ishaq M. Efficacy of intravitreal bevacizumab combined with pan retinal photocoagulation versus panretinal photocoagulation

3. Gao S, Lin Z, Shen X. Anti-vascular endothelial growth factor therapy as an alternative or adjunct to pan-retinal photocoagulation in treating proliferative diabetic retinopathy: meta-analysis of randomized trials. *Frontiers in Pharmacology*. 2020 Jun 5;11:849.
4. Huang CX, Lai KB, Zhou LJ, Tian Z, Zhong XJ, Xu FB, Gong YJ, Lu L, Jin CJ. Long-term effects of pattern scan laser pan-retinal photocoagulation on diabetic retinopathy in Chinese patients: a retrospective study. *International journal of ophthalmology*. 2020;13(2):239.
5. Mansour AM, Khalil El Jawhari J. Role of peripheral pan-retinal photocoagulation in diabetic macular edema treated with intravitreal ziv-aflibercept. *Clinical Ophthalmology (Auckland, NZ)*. 2019;13:695.
6. Park N, Lee IG, Kim JT. Changes in choroidal thickness in advanced diabetic retinopathy treated with pan-retinal photocoagulation using a pattern scanning laser versus a conventional laser. *BMC ophthalmology*. 2020 Dec;20(1):1-7.
7. Ahmed T, Howaidy A, El-Amin AA, Selim K. PASCAL laser produces less pain responses compared to conventional laser system during the panretinal photocoagulation. *The Egyptian Journal of Hospital Medicine*. 2020 Jan 1;78(1):110-4.
8. Ahmed T, Howaidy A, El-Amin AA, Selim K. Effect of Diabetes Duration on Proliferative Disease Regression after Panretinal Photocoagulation Using a Conventional Laser Versus Pattern Scan Multispot Laser. *The Egyptian Journal of Hospital Medicine*. 2020 Jan 1;78(1):123-7.
9. Sun C, Zhang HS, Yan YJ, Zhao T, Li AH, Tang Y, Wang ZJ. Early vitrectomy combined with pan retinal photocoagulation, anti-vascular endothelial growth factor, and gradual cyclophotocoagulation for treatment of neovascular glaucoma. *Chinese Medical Journal*. 2019 Oct 20;132(20):2518-20.
10. Soleimani A, Rasta SH, Banaei T, Bonab AA. Effects of laser physical parameters on lesion size in retinal photocoagulation surgery: clinical OCT and experimental study. *Journal of biomedical physics & engineering*. 2017 Dec;7(4):355.
11. Reddy SV, Husain D. Panretinal photocoagulation: a review of complications. In *Seminars in ophthalmology 2018* Jan 2 (Vol. 33, No. 1, pp. 83-88). Taylor & Francis.
12. Polat O, Inan S, Baysal Z, Yigit S, Inan UU. Comparison of navigated laser and conventional single-spot laser system for induced pain during panretinal photocoagulation. *Lasers in Medical Science*. 2020 Apr;35(3):687-93.
13. Lorusso M, Milano V, Nikolopoulou E, Ferrari LM, Cicinelli MV, Querques G, Ferrari TM. Panretinal photocoagulation does not change macular perfusion in eyes with proliferative diabetic retinopathy. *Ophthalmic Surgery, Lasers and Imaging Retina*. 2019 Mar 1;50(3):174-8.
14. Elsawah KM, El-Ikwa AF, El-Abedin GZ, Zaky MA. Comparison between multi-spot laser and conventional laser in treatment of diabetic clinically significant macular edema. *Revista Brasileira de Oftalmologia*. 2017 Jul;76:175-80.
15. Vijayan ME, Jose RO, Abraham SU, Joy JI. Study on quality of life assessment in diabetic retinopathy among patients with type 2 diabetic patients. *Asian J Pharm Clin Res*. 2017;10(7):116-9.
16. Moutray T, Evans JR, Lois N, Armstrong DJ, Peto T, Azuara-Blanco A. Different lasers and techniques for proliferative diabetic retinopathy. *Cochrane Database of Systematic Reviews*. 2018(3).
17. Huang S, Curragh D, Selva D, Davis G. Posterior Ischemic Optic Neuropathy Following Contralateral Endoscopic Orbital Decompression. *Ophthalmic Plastic & Reconstructive Surgery*. 2018 Nov 1;34(6):598-9.

18. Mistry H, Auguste P, Lois N, Waugh N. Diabetic retinopathy and the use of laser photocoagulation: is it cost-effective to treat early?. *BMJ open ophthalmology*. 2017 Sep 1;2(1):e000021.
19. Abdelmotaal H, Ibrahim W, Sharaf M, Abdelazeem K. Causes and clinical impact of loss to follow-up in patients with proliferative diabetic retinopathy. *Journal of Ophthalmology*. 2020 Feb 8;2020.
20. He F, Yu W. Longitudinal neovascular changes on optical coherence tomography angiography in proliferative diabetic retinopathy treated with panretinal photocoagulation alone versus with intravitrealconbercept plus panretinal photocoagulation: a pilot study. *Eye*. 2020 Aug;34(8):1413-8.
21. Seewoodhary M. An overview of diabetic retinopathy and other ocular complications of diabetes mellitus. *Eye*. 2020.
22. Patrycia F, Virgana R. Effect of Panretinal Photocoagulation on Color Vision in Diabetic Retinopathy.
23. Elsawah KM, El-Ikwa AF, El-Abedin GZ, Zaky MA. Comparação entre laser multi-spot e laser convencional no tratamento de edema macular diabético. *Revista Brasileira de Oftalmologia*. 2017 Aug;76(4):175-80.