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Original Article

Quantification of Inflammation Following Neodymium Yttrium Aluminum Garnet (Nd:YAG) Laser Capsulotomy and Assessing the Anti-Inflammatory Effects of Nepafenac 0.1 % & Pred Forte 1%

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ABSTRACT

Objectives: To quantify intraocular inflammation following Nd:YAG Laser capsulotomy and compare the effectiveness of topical non-steroidal and steroidal anti-inflammatory medication to reduce post-capsulotomy inflammation.
Study Design: Quasi-experimental study.
Place and Duration of Study: Armed Forces Institute of Ophthalmology, Rawalpindi Pakistan, from Jan to Jun 2023.
Methodology: The patients were divided into two groups, on the basis of topical medication prescribed as per ophthalmologist's discretion. Group-A was administered topical steroid drug (Pred Forte eye drops, Prednisolone Acetate 1%) and Group-B was administered non-steroidal anti-inflammatory drug (Nepac eye drops, Nepafenac 0.1%). Following Nd: YAG laser treatment, every patient was examined at 2 hours, 1 week, and 2 weeks to assess best corrected visual acuity, intraocular pressure and central macular thickness.
Results: There were 94 patients (47 in each group) with mean age of 52.1±7.3 years. There were 46(48.9%) males and 48(51.1%) females. Best corrected visual acuity was found to improve following Nd:YAG in all the patients. The inflammation was found to rise acutely after procedure and gradually decreased till 2 weeks post-procedure. The optical parameters were found to rise slightly after procedure but were self-limiting in nature. Non-steroidal anti-inflammatory drug was found to be more effective in preventing the ocular inflammation as compared to steroid drug.
Conclusion: The topical nonsteroidal anti-inflammatory drugs were found to be slightly better at lowering post-capsulotomy inflammation compared to topical steroids. This suggests NSAIDS as a viable treatment option for post-capsulotomy intraocular inflammation.

Keywords: Cataract Extraction, Capsule Opacification, Capsulotomy, Posterior Capsular Opacification, YAG Capsulotomy, Inflammation.

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INTRODUCTION

One of the most frequent problems following cataract surgery is posterior capsular opacification, the prevalence of which is reported to range from 8.7% to 33.4%.[1,2] For posterior capsular opacification, Neodymium Yttrium Aluminum Garnet (Nd:YAG) laser capsulotomy is the best method for treating it, with 95% success rate.[3] After cataract surgery, visual impairment occurs frequently due to posterior capsular opacification despite the development of better surgical procedures like phacoemulsification and newer intraocular lens materials and designs.[4]

Although noninvasive, Nd:YAG laser capsulotomy procedure leads to a number of side effects, including corneal injury, iritis, hyphema, pupil blockade, pitting of intraocular lens, intraocular lens dislocation, vitritis, macular edema, and retinal detachment.[5-7] Slit lamp examination can be used by ophthalmologists to grade parameters of anterior chamber inflammation and laser flare photometry further aids to assess and quantify the parameters of inflammation. Laser flare photometry is the sole technique that can reliably, correctly, and objectively quantify intraocular inflammation. After surgery, Nd:YAG laser capsulotomy induces inflammation[8,9] Availability of laser flare photometry is quite limited especially in developing countries thus ophthalmologists have to rely upon slit lamp examination to grade the extent of ocular inflammation. The exact course and intensity of ocular inflammation after Nd:YAG Laser capsulotomy are not well understood as only a small number of studies have been published that have estimated inflammation of anterior chamber after this procedure.[10]

Not much literature is available to conclusively support the efficacy of topical steroidal and nonsteroidal anti-inflammatory medications to

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subside inflammation post laser capsulotomy. There is a need to explore the best available treatment options to lower the post-capsulotomy inflammation among patients. In the light of that, quantify the development of ocular inflammation following Nd: YAG laser capsulotomy, and to assess the effectiveness of topical non-steroidal and steroidal anti-inflammatory drops to reduce the inflammation, a quasi-experimental study was conducted.

METHODOLOGY

This quasi-experimental study was conducted at Armed Forces Institute of Ophthalmology Rawalpindi Pakistan for a period of six months from January to June 2023. The study protocol was approved from Institutional Ethical Review Board (Approval no. 289/ERC/AFIO) before starting the data collection. The minimum sample size of 94 (47 in each group) was calculated for this study. Calculations were done using WHO sample size calculator, keeping 95% level of confidence, 80% power, 10% precision, 1.76 effect size for inflammation reduction using non-steroidal drugs, and pooled standard deviation of 3.0.[11]

Inclusion Criteria: All patients with age more than 30 years, having visually significant posterior capsular opacification, that developed subsequently after implantation of intraocular lens in posterior chamber and then electively planned for Nd:YAG laser capsulotomy procedure were included in the study.

Exclusion Criteria: Patients with other ocular media opacities, recent history of use of topical steroidal or non-steroidal anti-inflammatory drugs, other existing ocular, corneal or vitreoretinal diseases, comorbidities including diabetes, hypertension, pulmonary or cardiac diseases, or allergy to topical anti-inflammatory drugs were excluded from enrolment to eliminate confounding factors that might influence the outcome of study and to determine the true effect of intervention on optical parameters considered in the study.

All the patients considered for enrolment were voluntarily consented for participation in the study. Using non-probability convenience sampling technique, the patients were divided into two groups, on the basis of prescribed drug. The drug was prescribed as per ophthalmologist's discretion. Group-A was administered topical steroidal anti-inflammatory drug (Pred Forte eye drops, Prednisolone Acetate 1%) and Group-B was administered non-steroidal anti-inflammatory drug (Nepac eye drops, Nepafenac 0.1%). Before undergoing the elective Nd:YAG Laser capsulotomy procedure, the baseline demographic data was recorded for all the patients, and ophthalmic examinations were also done including best corrected visual acuity, intraocular pressure measurement and anterior chamber examination via slit lamp. To evaluate posterior capsular opacification and to perform ocular examination, Tropicamide (0.8%) ophthalmic drops were used to dilate the pupils. Optical coherence tomography (OCT) was done to measure the central macular thickness using Heidelberg Spectralis OCT.

Under topical anaesthesia, Nd:YAG laser capsulotomy was done by using Abraham capsulotomy lens, Brunswick. Mean spots of 24±11 were applied using laser spots with an energy of 1.8-4.2 mJ. Following allocation of patients to one of the two study groups, post-laser topical drops were administered in accordance with the ophthalmologist's decision. Group-A was administered topical steroid (Prednisolone Acetate 1%, Pred Forte) after every 8 hours for two weeks plus treatment as usual, Group-B was administered non-steroidal anti-inflammatory drops (Nepafenac 0.1%) after every 8 hours for two weeks plus treatment as usual. Treatment as usual included anti-glaucoma drops (topical Timolol Maleate 0.5% medication) 12 hourly for duration of two weeks. Following laser treatment, every patient was examined at 2 hours, 1 week and 2 weeks. This timeline of follow-up was chosen to monitor early and late post-procedure inflammation determined in terms of optical parameters decided for our study. Best corrected visual acuity (BCVA) measurement, intraocular pressure (IOP) measurement, ocular anterior and posterior segment examination and central macular thickness (CMT) measurement were all included in post-procedure follow up examination at each timepoint. BCVA refers to the clearest vision that a person can achieve with the use of corrective lenses under optimal lighting conditions, it is measured in LogMAR (Logarithm of the Minimum Angle of Resolution) scale to report the visual acuity; IOP represents the force exerted by the fluid within the eye against the walls of the eye, primarily the cornea and the sclera and is measured in millimeters of mercury (mmHg); the anterior segment examination refers to the clinical assessment of the anterior segment of eye, including

the cornea, anterior chamber cells and flare, iris, pupil, crystalline lens and the ciliary body, examined by a slit-lamp biomicroscope; AC cells (counted using 1mm by 1mm slit beam) and AC flare are both graded (grades 0 to 4+) with slit lamp examination under standardized lighting and magnification according to Standardization of Uveitis Nomenclature (SUN) criteria; the posterior segment examination refers to the examination of the posterior segment of the eye, which includes the vitreous body, retina, optic nerve head, and the choroid, examined with the help of Super Field Lens via slit-lamp biomicroscope; CMT is the retinal thickness at center of the macula, mainly within an area of 1 mm diameter at the fovea, measured in micrometers (µm) using optical coherence tomography (OCT).

Data was entered and analyzed using IBM SPSS software (version 23.0). Normality of data was checked visually by histogram, and statistically by Shapiro-wilk test. All quantitative variables were normally distributed. Descriptive statistics were performed initially followed by inferential statistics. Mean and standard deviation presented continuous data, while frequency and percentages were used to represent categorical data. The optical parameters including visual acuity, intraocular pressure and central macular thickness were taken at multiple time points (baseline, post-procedure hour-2, week-1 and week-2) and were compared for both Group-A and Group-B using repeated measure ANOVA test. The mean anterior chamber (AC) cells and anterior chamber (AC) flare values were compared between groups at baseline, post-procedure hour-2, week-1 and week-2 using independent samples t-test. A *p*-value of ≤0.05 was considered statistically significant.

RESULTS

The study comprised of 94 patients, where half of the patients were administered topical steroidal drug (Group-A) after procedure while remaining half were administered topical non-steroidal anti-inflammatory drug (Group-B). The patient flow diagram is given as figure-1. The overall mean age was calculated to be 52.1±7.3 years, whereas mean age among groups was 53.2±7.5 years and 51.8±7.9 years for Group-A and Group-B, respectively. There were 46(48.9%) males and 48(51.1%) females overall, while among Group-A there were 21(44.7%) males and 26(55.3%) females and among Group-B there were 25(53.2%) and 22(46.8%) males and females, respectively. The baseline demographic and clinical characteristics are summarized in Table-I. The baseline characteristics were similar for both study groups, except central macular thickness which was slightly higher in Group-A.

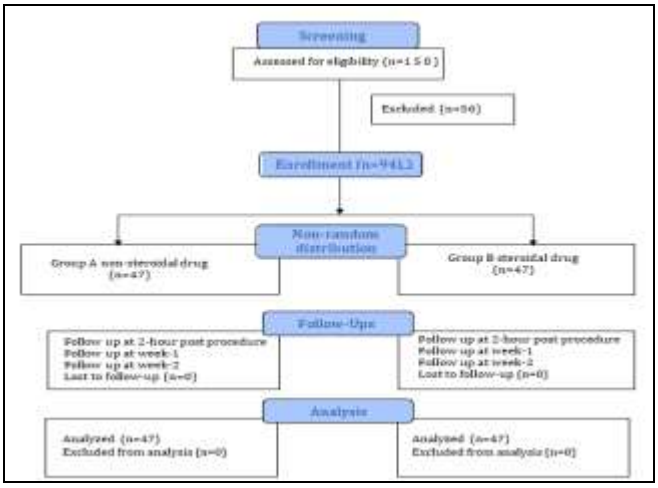

Figure-1: Patient flow diagram

Table-I: Summary of Demographic and Clinical Characteristics of Study Participants (n=94)

Characteristic(s)	Overall (n=94)	Study Groups		*p*-value
		Group-A Steroid drug (n=47)	Group-B Non-steroidal drug (n=47)	
Age (years)	52.1±7.30	53.2±7.50	51.8±7.90	1.000
Gender				
Male	46(48.9%)	21(44.7%)	25(53.2%)	0.409
Female	48(51.1%)	26(55.3%)	22(46.8%)	
Pre-procedure VA	0.91±0.22	0.89±0.25	0.93±0.20	0.370
Pre-procedure IOP	17.11±3.20	17.41±3.30	16.85±3.10	0.324
Pre-procedure CMT	328.82±19.7	333.31±18.2	324.31±20.3	0.026
Power used during procedure	2.94±0.91	2.85±0.87	3.05±0.92	0.225

VA: Visual Acuity, IOP: Intra Ocular Pressure, CMT: Central Macular Thickness

Preoperative parameters including best corrected visual acuity, intraocular pressure and central macular thickness were compared with those at follow up at hour-2, week-1 and week-2 as given in Table-II. Significant differences were noted in the mean visual acuity reported in patients belonging to Group-A and Group-B at various time points. The mean visual acuity at baseline was lesser as compared to the visual acuity at hour-2, week-1 and week-2 in both the groups. The mean intraocular pressure increased from baseline to hour-2 post-procedure, while it reduced at follow up week-1 and further reduced at week-2, similar trend was observed in both study groups. The mean value of central macular thickness on the other hand

remained same at hour-2 post-procedure, while it increased at week-1 and again decreased at week-2 timepoint, similar trend was observed in Group-A and Group-B.

Table-II: Comparison of Optic Parameters Pre- and Post-Procedure Among Study Groups (n=94)

Parameter(s)		Study Groups			
		Group-A Steroid Drug (n=47)	*p*-value	Group-B Non-steroidal drug (n=47)	*p*-value
Visual acuity (VA)	Pre-procedure	0.89±0.25	<0.001	0.93±0.20	<0.001
	Hour-2	0.66±0.28		0.71±0.22	
	Week-1	0.22±0.31		0.27±0.27	
	Week-2	0.19±0.30		0.14±0.25	
Intraocular pressure (IOP)	Pre-procedure	17.40±3.31	<0.001	16.80±3.11	<0.001
	Hour-2	20.52±5.62		19.11±4.62	
	Week-1	19.81±3.14		17.92±3.64	
	Week-2	16.95±2.62		17.15±2.86	
Central macular thickness (CMT)	Pre-procedure	333.32±18.15	<0.001	324.33±20.31	<0.001
	Hour-2	333.34±18.14		324.32±20.38	
	Week-1	352.35±18.48		335.74±18.87	
	Week-2	333.10±16.66		328.02±18.20	

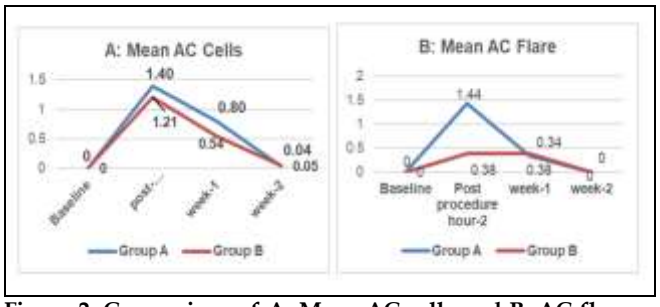

Figure-2: Comparison of A: Mean AC cells and B: AC flare at various timepoints in Group-A and B

Table-III: Comparison of AC Cells and AC Flare Parameters at Pre-Procedure, Post-Procedure Hour-2, Week-1 And Week-2 Follow Ups Post-Procedure Between Two Groups (n=94)

Parameters		Group-A Steroid drug (n=47)	Group-B Non-steroidal drug (n=47)	*p*-value
AC cells	Pre-procedure	0.00±0.00	0.00±0.00	-
	FU at Hour-2	1.40±0.85	1.21±0.67	0.232
	FU at Week-1	0.80±0.66	0.54±0.49	0.031
	FU at week-2	0.04±0.14	0.05±0.15	0.729
AC flare	Pre-procedure	0.00±0.00	0.00±0.00	-
	FU at Hour-2	1.44±0.50	0.38±0.49	<0.001
	FU at Week-1	0.34±0.47	0.38±0.49	0.672
	FU at week-2	0.00±0.00	0.00±0.00	-

AC: Anterior Chamber FU: Follow Up

The AC cells and AC flare parameters were also compared at various timepoints between Group-A and Group-B. At baseline the AC cells and AC flare was zero among both study groups. At post-procedure hour-2, it was reported that the mean AC cells were slightly higher in topical steroidal drug Group-A as compared to Group-B but the difference was not statistically significant (p=0.232). At post-procedure week-1, the mean number of AC cells was significantly lower in Group-B as compared to Group-A (0.54±0.49 vs 0.80±0.66 cells, p=0.031). At week-2 following post-procedure, the number of mean AC cells fell to grade 0, almost similar in both Group-A and Group-B with no significant difference. There was a significant difference noticed in mean AC flare reading at post-procedure hour-2 where the value was significantly lower in Group-B as compared to Group-A (0.38±0.49 vs 1.44±0.50, p<0.001). Whereas, at week-1 following the procedure, same mean AC flare was noted in both the groups with no significant difference as shown in Table-III. The trends of AC cells and AC flare at different time points in two groups are given in figure-2.

DISCUSSION

This study was conducted with an objective to quantify intraocular inflammation after Nd:YAG Laser capsulotomy and assess the effectiveness of topical non-steroidal and steroidal anti-inflammatory medication in the reduction of inflammation following Nd:YAG Laser capsulotomy. The inflammation was assessed among 94 participants in terms of AC cells and AC flare, that was found to rise acutely after procedure and gradually decreased till 2 weeks post-procedure. The optical parameters including IOP and CMT were found to rise only slightly after procedure but were self-limiting in nature among both groups of steroidal and non-steroidal drugs. Topical non-steroidal anti-inflammatory drug was found to be slightly more effective in the prevention of ocular inflammation in comparison to topical steroid drug.

There is controversy in establishing the effectiveness of topical NSAIDs over topical steroid drops in treating post-procedure inflammation in literature.[12-14] In clinical practice, these drugs can be used alone or in combination. Usually, it's up to ophthalmologist's discretion if he prescribes a combination of two or a single topical anti-inflammatory drug based on his experience and knowledge.

A trial conducted in 2019 by Jinagal J *et al.*,[15] to quantify the intraocular inflammation by using the laser flare photometry following Nd:YAG capsulotomy procedure included 90 patients who were divided into three study groups on the basis of steroid drug, non-steroidal drug and control group. The authors noted a significant increase in the mean

laser flare photometry value two hours following Nd:YAG Laser capsulotomy procedure, showing a gradual decline with time reaching baseline within 2-weeks. In comparison to the control group, the study groups prescribed with anti-inflammatory drugs were more likely to recover from inflammation in less duration, but overall there was no significant difference reported.[15] Similarly in the current study, where there was no sign of any inflammation, marked inflammation was recorded on hour-2 following the Nd:YAG capsulotomy procedure in both study groups. The inflammation resolved within 2-weeks post-procedure, as reported by Jinagal *et al.,* and reached gradually to baseline in study groups. In our study, we noticed an increase in inflammation parameters between study groups measured in terms of AC cells (p=0.03) and AC flare (p<0.001) at week-1 where high inflammation parameters were noticed in topical steroid group as compared to topical non-steroidal anti-inflammatory drug. Inflammatory parameters returned back to the baseline values at week-2 in both study groups equally.

Atilgan CU *et al.,*[16] compared topical steroid and non-steroid drugs with a control group for macular thickness after Nd:YAG laser capsulotomy. Both drugs prevented post-procedural macular thickening with no significant difference between them. In our study, macular thickness remained stable at hour-2 and week-1 but slightly increased at week-2, with a moderate, non-significant difference (p=0.155) favoring non-steroids. A cohort study conducted by Hecht I *et al.,*[16] analyzed 25,818 patients who underwent cataract surgery and currently were elected for Nd:YAG laser capsulotomy, to determine the role of drugs on post-surgery inflammation. The authors reported that when compared to topical non-steroidal anti-inflammatory drug-only treatment, post-surgery topical steroid administration was linked to decreased incidence of clinically significant posterior capsular opacification in individuals undergoing straightforward cataract surgery, while the topical steroid and NSAID combination therapy did not provide any advantages over steroid therapy alone.[17] In current study anti-inflammatory effects of non-steroidal eye drops were found to be slightly more significant in comparison to steroid eye drops, in terms of reduction in post-procedure intraocular inflammation.

Another study by Deshwal M *et al.,*[18] was conducted to compare the effect of combination of topical steroid and non-steroid drug with steroid alone on macular thickness following Nd:YAG laser capsulotomy. The authors reported that at one-hour post-procedure, the mean increase in IOP in both groups was statistically significant; at one week and six weeks, it returned to non-significant levels, while the CMT remained same in both the groups. It was concluded that prescription of topical steroid or non-steroid drugs are not needed in patients receiving Nd: YAG laser capsulotomy, as no signs of cystoid macular oedema were found at follow ups. In current study we noticed similar findings that the post-operative rise in intraocular pressure was similar in both study groups and it was noticed to be slightly higher in steroid drug group in comparison to non-steroid drug group but this difference was not significant, and the values returned to baseline values at 2-weeks.

Literature presents mixed views on the benefits of topical steroids, NSAIDs, and their combination for reducing post-Nd:YAG laser capsulotomy inflammation in cataract patients. Some studies favor steroids, others NSAIDs, while some support both. Insufficient evidence exists to determine the best approach, with differing perspectives for adult and pediatric patients.[15] In the current study we had a limitation of having only two study groups, one administering topical steroid drug while other administering topical non-steroid drug, whereas control group comparison and combination of two drugs were not explored in this study. Another limitation was that the sample was taken from single-center only, randomization was not employed to divide patients in groups that can lead to selection bias therefore the results might not be generalizable to wider population. Confounding variables such as hypertension and diabetes that might influence the outcomes were not addressed in current study. In this study we used slit lamp to examine and grade the inflammatory parameters, which would be captured with more accuracy using the laser flare photometry that was not available at our center. The current study supports the use of both topical steroid and non-steroid drugs, but the evidence favours non-steroidal anti-inflammatory drugs a little bit more based on the course of inflammatory parameters studied during follow up visits of patients.

CONCLUSION

Following Nd:YAG laser capsulotomy, a temporary intraocular inflammation was noticed. The topical nonsteroidal anti-inflammatory drugs were found to be slightly better at lowering intraocular inflammation as compared to topical steroids.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AI & WM: Data acquisition, data analysis, critical review, approval of the final version to be published.

SN & JA: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

AP & RH: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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