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A Study to Compare The Efficacy of 0.5% Timolol Eye Drops Versus 0.2% Brimonidine Eye Drops in Management of Rise In Iop Following Nd-Yag Capsulotomy

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Abstract:
Aims: *A Study to compare the efficacy of 0.5 % Timolol eye drop's vs. 0.2% Brimonidine eye drops in management of rise in Intra Ocular Pressure following neodymium-yttrium aluminium garnet (YAG) capsulotomy for Posterior Capsular Opacification.*
Settings And Design: *It's a Non randomized study, conducted in the Ophthalmology Department of Coimbatore Medical College Hospital which is a tertiary care Hospital and Major reference centre.*
Materials And Methods: *100 Nonglaucomatous patients in the age group between 40 to 70 years having posterior capsular opacification, who have had cataract surgery more than six months visiting the Out Patient in the Department of Ophthalmology were included in the study. 50 of these patients were given 1 drop of 0.5% Timolol eye drops 1 hour before the procedure and I drop after the procedure and were advised to use 0.5 % Timolol eye drops twice a day for the next 7 days . The remaining 50 of these patients were given 1 drop of 0.2% Brimonidine eye drops 1 hour before the procedure and I drop after the procedure and were advised to use 0.2% Brimonidine eye drops twice a day for the next 7 days .*
Results: *In our study both 0.2 % Brimonidine and 0.5 % Timolol are effective in management of rise of IOP following Nd YAG capsulotomy. Our study concludes that Topical Brimonidine eye drops controls the transient rise in IOP better than Timolol following ND YAG Capsulotomy.*
Keywords*: Posterior capsular opacification, Nd YAG laser, Timolol, Brimonidine*

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I. Introduction

Posterior capsular opacification (PCO) is a frequent complication of cataract surgery with posterior chamber intraocular lens (PCIOL) implantation. Nd: YAG laser posterior Capsulotomy is the treatment of choice for the PCO. Raised intraocular pressure (IOP) remains to be one of the frequent complications of Nd: YAG laser capsulotomy. It is acute but transient. The efficacy of of 0.5 % Timolol eye drop's vs. 0.2% Brimonidine eye drops in monitoring rise in IOP following Nd-YAG Capsulotomy was analysed in our study.

Subjects And Methods

Study design: The study design of this study was a Nonrandomized hospital based study. Pseudophakic patients with posterior chamber IOL's having poor vision due to PCO who have had a cataract surgery more than six months visited our outpatient from August 2013 to July 2014 were included in our study. Patients with Corneal diseases with hazy media, Inflammatory eye diseases, Glaucoma, Less than 3 months post cataract surgery, Posterior segment surgery, Trabeculectomy, Macular oedema/ maculopathy, High Myopia more than 6 D were excluded from our study.

An increase in IOP of >5 mmHg from the baseline (prelaser capsulotomy) after Nd: YAG laser posterior capsulotomy was termed as having '**raised IOP'**. Energy used in this procedure was termed as 'low energy' if it was less than 30mJ and **'high energy'** if it was >30mJ. 100 patients with PCO were studied for post ND: YAG laser rise in IOP. The patient not having any organic cause of decreased vision and who have completed at least three months after cataract surgery were selected. Pachymetery was used to measure the central corneal thickness and the corrected IOP was measured 1 hour, 4 hours, 3rd day, and 7th day following the procedure.

Method: The Name, age, gender, address and contact number of all the selected patients having PCO, was collected**.** Before performing Nd:YAG laser posterior capsulotomy, all patients underwent a thorough ophthalmic evaluation including the Best corrected visual acuity (BCVA), Slit lamp examination, IOP measurement by Goldmann Applanation tonometer and NCT, Detailed fundus examination to rule out any pre-existing pathology. The pupil was dilated with 1% tropicamide eye drops.1 drop of 0.5%Timolol eye drops was instilled in 50 patients 1 hour before Nd: Yag Capsulotomy.1 drop of 0.2 % Brimonidine eye drops was instilled

in 50 patients 1 hour before Nd: Yag Capsulotomy. Proparacaine hydrochloride eye drops was used for topical anaesthesia, one drop 1-2 times about 2-3 minutes before applying contact lens (ABRAHAM CAPS YAG LENS). Nd:YAG laser was used for capsulotomy. The power in mJ and the number of shots was individualised for each patient based on the thickness of PCO. An opening of 3-4 mm was made in the posterior capsule by o**ne single consultant ophthalmologist**, using minimum possible pulses of Nd: YAG laser. The total amount of energy used in YAG laser capsulotomy procedure was noted, as viewed on the control display panel of Nd:YAG laser machine, and was recorded.

1 drop of 0.2 % Brimonidine eye drops was instilled in 50 patients following the procedure. The patients in the Brimonidine group were advised to apply 0.2% Brimonidine eye drops twice a day for 7 days after the procedure. 1 drop of 0.5%Timolol eye drops was instilled in 50 patients of the 2ndcomparision group following the procedure.The patients in the Timolol group were advised to apply 0.5% Timolol eye drops twice a day for 7 days after the procedure. The IOP was measured 1 hour, 4 hours, 3rd day, and 7th day following the procedure.

Statistical Analysis

The collected data was analysed with **SPSS 16.0 version**. To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and for continuous variables the mean and S.D were used. To find the significance difference between the bivariate samples in Paired groups (NCT & AT prior) Paired sample t-test was used & for Independent groups (Timilol & Brimonidine) Independent t-test was used. For the repeated measures (AT -Prior, Hour 1,Hour 4,Day 3 & Day 7) the Repeated measures of ANOVA with adjustment for multiple comparisons to control the type I error, the **Bonferroni test** was used. To assess the relationship between the variables **Pearson's Correaltion** was used.To find the significance in categorical data **Chi-Square test** was used. In all the above statistical tools the probability value .**05 is considered as significant level**.

Sex Wise Distribution

Among the 100 patients selected randomly for the study 45 were males and remaining 55 were females.

Age Wise Distribution

Among the 100 patients selected for the study 22 of them were between the age group of 40-55 years,43 patients were in the age group of 56- 65 years, 26 patients were in the age group of 66 to 75 years and 9 of the patients were above 75 years. The descriptive statistics i.e., frequency analysis for this study revealed that the minimum age of the patient selected for the study was 40 years and maximum age was 83 years the mean for the 100 patients was calculated as 63.19 and the standard deviation from the mean was noted as 9.530

Best Corrected Visual Acuity (BCVA) of the patient was checked with a pin hole before ND YAG laser capsulotomy The fundus examination of the 100 patients before the procedure showed the fundus within normal limits with a very hazy view due to the posterior capsular opacification. The Intraocular Pressure was measured using a Non Contact Tonometer 1 hour prior to ND YAG Capsulotomy both in the Timolol and Brimonidine group it was found out that the mean IOP in Timolol group patients was 16.24 and in the Brimonidine group patients the mean was calculated to be 15.76. A paired t test was applied to study the IOP with NCT and with AT 1 hour prior to the procedure , the mean IOP using NCT in the 100 patients was found out to be 16.0 and the standard deviation was calculated as 2.6515 and IOP with AT was 17.16 with a standard deviation of 2.719. The study showed a **P = 0.0001** which indicates that a significant statistical difference exists between the IOP measured with NCT and AT.

Number Of Shots Of Nd: Yag Laser

The average number of shots of Nd YAG laser in the Timolol group and Brimonidine group was found to be 9.20 and 9.40 respectively. The mean of the total energy delivered in the timolol group and Brimonidine group was found to be 35.60 and 35.34 respectively. **Above 30 mJ** was taken as high energy in our study, in the Timolol group in 21 patients and in Brimonidine group 16 patients had high energy delivered . 21 patients in timolol group and 16 patients in Brimonidine group less than 30 mJ of energy was delivered.

Chi Square Test was applied to study the relationship between the energy used and the rise in IOP . It was found out that **P=.300** indicating that the total energy delivered did not have any relationship with rise in IOP. In the Timolol group the mean IOP measured with AT 1 hour prior to Nd YAG laser Capsulotomy was 17.4 with a SD of 2.49 , the mean IOP measured 1 hour after the procedure was 21.6 with a SD of 2.84 , mean IOP after 4 hours was 18.6 with a SD of 2.99 , the mean IOP on the 3rd and the 7th day was recorded as 17.6 and 17.5 respectively and with a SD of 2.61 and 2.66 respectively.

Table 1: Shows the descriptive statistics for Timolol Group

AT	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	17.444	.352	16.737	18.151
2	21.620	.402	20.812	22.428
3	18.612	.422	17.763	19.461
4	17.596	.369	16.854	18.338
5	17.476	.377	16.719	18.233

In the Brimoidine group the mean IOP measured with AT 1 hour prior to ND YAG laser Capsulotomy was 16.9 with a SD of 2.93 , the mean IOP measured 1 hour after the procedure was 20.2 with a SD of 2.96 , mean IOP after 4 hours was 17.4 with a SD of 2.84 , the mean IOP on the 3rd and the 7th day was recorded as 16.8 and with a SD of 2.93 .

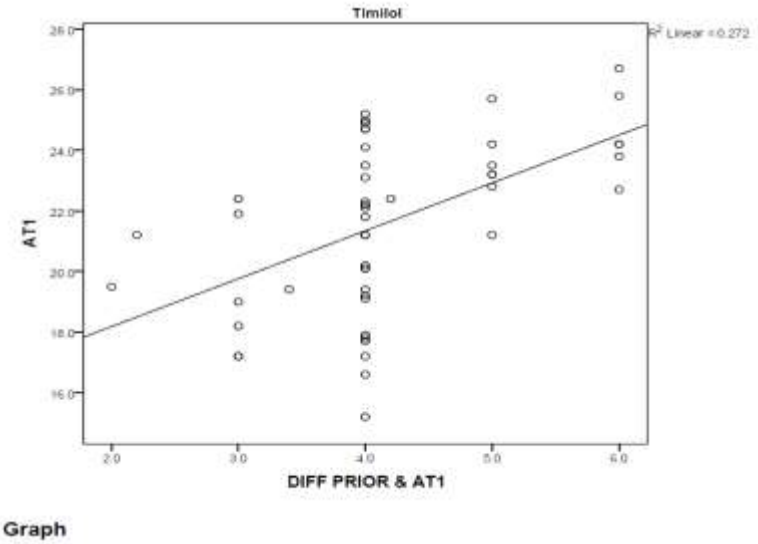
Table 2: Shows the descriptive statistics fot Brimonidine Group

AT	Mean	Std. Error	95% Confidence Interval	
			Lower Bound	Upper Bound
1	16.876	.415	16.043	17.709
2	20.198	.419	19.356	21.040
3	17.438	.403	16.629	18.247
4	16.878	.415	16.045	17.711
5	16.878	.415	16.045	17.711

The mean IOP with AT 1 hour prior to procedure in Timolol group was 17.44 while in the Brimonidine group it was 16.9. The mean IOP with AT 1 hour after the procedure in Timolol group was 21.6 while in the Brimonidine group was 20.2 . There was a significant rise in mean IOP by 4.2 in the Timolol group while in the Brimonidine group the rise in the mean IOP was 3.3 mm 1 hour after the procedure.

The mean IOP with AT 4 hours after the procedure in Timolol group was 18.6 while in the Brimonidine group it was 17.4 . The rise in mean IOP after 4 hours in the timolol group was 1.2 mm and 0.5 mm in the Brimonidine group.

The mean IOP with AT 3rd day after the procedure in Timolol group was 17.6 while in the Brimonidine group it was 16.9. The mean IOP with AT 7th day after the procedure in Timolol group was 17.5 while in the Brimonidine group was 16.9. The comparison between Timolol and Brimonidine in AT1 shows that there is high statistical difference at P = .016 ≤ .01 level with the mean ± S.D of Timilol (21.62 ± 2.84) and Brimonidine(20.19 ± 2.96). The P value was **0.016** which was statistically very significant. From the above analysis the mean rise in IOP in Timolol group was 4.18 mm Hg compared to Brimonidine group for which it was 3.32 mm Hg. This shows that Brimonidine was better than Timolol in the management of rise of IOP following Nd Yag Capsulotomy and the rise in Intraocular Pressure was a Transient Phenomenon reaching its peak in the first 2 hours and subsiding after the 4th hour and normalising within the 3 rd Day.



Graph

Fig 1: Graph represents the relationship between mean IOP with AT 1 hour after the procedure and difference between the mean IOP 1 hour prior and 1 hour after AT in the Timolol group. The graph indicates a significant rise in the IOP after the procedure in the Timolol group . The relationship is linear and significant.

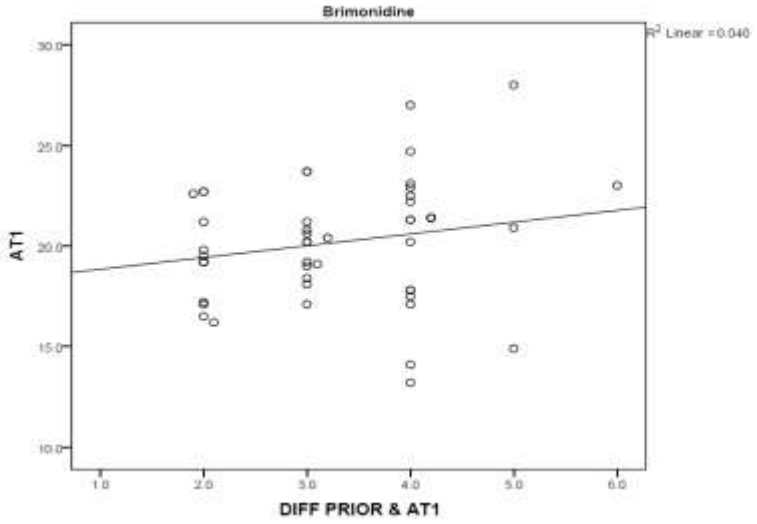


Fig 2: Graph represents the relationship between mean IOP with AT 1 hour after the procedure and difference between the mean IOP 1 hour prior and 1 hour after AT in the Brimonidine group. The graph indicates a significant rise in the IOP after the procedure in the Brimonidine group . The relationship is linear and less significant compared to Timolol.

TIMOLOL

Table 3: Correlations In Timolol Group

	DIFF PRIOR1	AT1	
DIFF PRIOR1	Pearson Correlation	1	.522**
	Sig. (2-tailed)		.0001
	N	50	50
AT1	Pearson Correlation	.522**	1
	Sig. (2-tailed)	.0001	
	N	50	50

**. Correlation is significant at the 0.01 level (2-tailed)

Chi square test for the Timolol group the IOP measured 1 hour prior and 1 hour after the procedure with AT showed a significant rise in IOP after the procedure with a P=0.0001.

BRIMONIDINE

Table 4: Correlations In Brimonidine Group

	DIFFPRIOR1	AT1	
DIFF PRIOR1	Pearson Correlation	1	.199
	Sig. (2-tailed)		.166
	N	50	50
AT1	Pearson Correlation	.199	1
	Sig. (2-tailed)	.166	
	N	50	50

Chi square test for the Brimonidine group the IOP measured 1 hour prior and 1 hour after the procedure with applanation tonometry showed a rise in IOP after the procedure with a P=0.166 . The study showed that the rise in IOP in Brimonidine group was not significant. Table 5: Represents the group statistics for the Timolol and Brimonidine group showing the Mean, Standard deviation, and Standard Error of Mean for the variables compared in the study. The comparison between Timilol and Brimonidine in AT1 shows that there is high statistical difference at P = .016 ≤ .01 level with the mean ± S.D of Timilol (21.62 ± 2.84) and Brimonidine(20.19 ± 2.96).

		Mean	Std. Deviation	Std. Error Mean
NCT	Timilol	16.240	2.5198	.3564
	Brimonidine	15.760	2.7816	.3934
SHOTS	Timilol	9.200	2.7180	.3844
	Brimonidine	9.400	3.0639	.4333
ENERGY	Timilol	4.024	2.2408	.3169
	Brimonidine	3.846	2.2283	.3151
TE	Timilol	35.598	21.0001	2.9699

	Brimonidine	35.342	22.0680	3.1209
AT PRIOR	Timilol	17.444	2.4860	.3516
	Brimonidine	16.876	2.9319	.4146
DIFF PRIOR1	Timilol	4.176	.9378	.1326
	Brimonidine	3.322	1.0066	.1424
AT1	Timilol	21.620	2.8427	.4020
	Brimonidine	20.198	2.9614	.4188
AT HR4	Timilol	18.612	2.9872	.4224
	Brimonidine	17.438	2.8478	.4027
AT DAY3	Timilol	17.596	2.6097	.3691
	Brimonidine	16.878	2.9313	.4146
AT DAY7	Timilol	17.476	2.6625	.3765
	Brimonidine	16.878	2.9313	.4146

Bcva Post

12 patients had no improvement in visual acuity ,60 patients had 1 snellen chart improvement , 23 patients had 2 snellen chart improvement, 5 patients had 3 snellen chart improvement. The Complications seen after ND YAG laser Capsulotomy 95 patients did not have any complications after the procedure , 4 patients had IOL pitting and 1 patient had Cystoid Macular Edema.

II. Discussion

Posterior Capsular Opcacification or after cataract is an frequent and nagging complication and an important cause of diminision of vision following Cataract Surgery. The incidence of PCO varies from 7 – 31 % 2 years post operatively. The main modality of management of PCO is Nd YAG Capsulotomy which consists of Neodymium Yttrium Aluminum Garnet crystal that produces parallel beam of Infra Red rays with a wavelength of 1064 nm which acts by photodisruption. Photo-disruption is accomplished by the acoustic wave generated by the plasma formed due to the high peak power pulse directed into the eye. As the energy is increased, the size of the plasma formed increases, thus causing a larger, stronger acoustic wave. Transient rise in IOP is a frequent and transient complication of ND YAG Capsulotomy which occurs as a consequence of obstruction of the outflow pathway by debris and macromolecules scattered by the laser treatment. Both Topical Brimonidine and Timolol can be effective in management of rise in IOP following **Nd YAG** Capsulotomy.This study compares the efficacy of Timolol and Brimonidine in managing the rise of IOP.

100 Patients in the age group between 40 to 70 years were selected study were matched in terms of age and sex. Among the 100 patients selected randomly for the study 45 were males and remaining 55 were females. The minimum age of the patient selected for the study was 40 years and maximum age was 83 years, the mean was 63.19 with a SD of 9.530.

The incidence of PCO (posterior capsule opacification) varies with different studies. Rates of posterior capsule opacification have been reported as 10–56% at 3 years with differing lens materials.[1]The incidence of posterior capsule opacification is lower if a meticulous cortical clean-up is performed.[2]**The** square lens edge designs hydrophobic acrylic lenses have been found to decrease posterior capsule opacification by decreasing the migration of lens epithelial cells.[3] The mitotic inhibitors when instilled into the anterior chamber after extracapsular cataract extraction have shown to reduce capsular opacification significantly.[4]The incidence of opacification at 3 years has been reported at 40% for silicone, 56% for polymethylmethacrylate, and 10% for acrylic material.[5]

The Intra Ocular Presure was measured using a Non Contact Tonometer 1 hour prior to Nd YAG Capsulotomy both in the Timolol and Brimonidine group it was found out that the mean IOP in Timolol group and Brimonidine group was calculated to be16.24 and 15.76 respectively.21 patients in the Timolol group and 16 patients in Brimonidine group > 30 mJ energy was delivered . Chi Square Test was applied to study the relationship between the energy used and the rise in IOP. It was found that P=.300 indicating that the total energy delivered did not have any relationship with rise in IOP. The risk of CME and retinal detachment may be greater when Nd:YAG capsulotomy is performed within 6 months of cataract surgery.[6] The safest approach is to focus the laser beam slightly behind the posterior surface of the capsule for the initial application and then move the subsequent applications anteriorly until the desired puncture is achieved. [7]The Nd:YAG capsulotomy leads to reduced facility of aqueous outflow by plugging the trabecular meshwork with inflammatory cells, capsular particles, ,and protein and by producing prostaglandin-mediated effects.[8] The "gradual IOP elevation or a need for more aggressive therapy is common in glaucoma patients following Nd:YAG laser posterior capsulotomy". It is unclear whether this progression is related directly to the Nd:YAG laser procedure or whether it is an independent progression of the patient's glaucoma unrelated to the Nd:YAG laser procedure .[9] The long-term IOP increase was significantly related to the IOP increase which was measured 1 hour after the capsulotomy (P =. 001). Patients with glaucoma required long-term additional glaucoma medication than non glaucoma patients after the capsulotomy (P =.002).[10]

The average number of shots of Nd YAG laser in the Timolol group and brimonidine group was found out to be 9.20 and 9.40 respectively. The mean of the total energy delivered in the timolol group and Brimonidine group was found to be 35.60 and 35.34 respectively.The total energy and number of laser pulses delivered do not appear to be contributing factors in the rise of IOP . In the Timolol group the mean IOP measured with Applanation Tonometry 1 hour prior to Capsulotomy was 17.4 with a SD of 2.49, the mean IOP measured 1 hour after was 21.6 with a SD of 2.84 , mean IOP after 4 hours was 18.6 with a SD of 2.99, the mean IOP on the 3rd and the 7th day was recorded as 17.6 and 17.5 respectively and with a SD of 2.61 and 2.66 respectively. In the Brimoidine group the mean IOP measured with Applanation Tonometry 1 hour prior to Capsulotomy was 16.9 with a SD of 2.93, the mean IOP measured 1 hour after the procedure was 20.2 with a SD of 2.96 , mean IOP after 4 hours was 17.4 with a SD of 2.84 , the mean IOP on the 3rd and the 7th day was recorded as 16.8 and with a SD of 2.93 .

The comparison between Timolol and Brimonidine in AT1 shows that there is high statistical difference at $P = .016 \leq .01$ level with the mean ± S.D of Timolol (21.62 ± 2.84) and Brimonidine (20.19 ± 2.96). The P value was **0.016** which was statistically very significant. From the above analysis the mean rise in IOP in the Timolol group and Brimonidine group was 4.18 and 3.32 mmHg. This shows that topical Brimonidine was better than Timolol in the management of rise of IOP following ND Yag Capsulotomy and the rise in Intraocular Pressure was a Transient Phenomenon reaching its peak in the first 2 hours and subsiding after the 4th hour and normalising within the 3 rd Day.

Chi square test for the Timolol group and Brimonidine group the IOP measured 1 hour prior and 1 hour after the procedure with applanation tonometry showed a significant rise in IOP after the procedure with a P=0.0001 and P=0.166 respectively. The study showed that the rise in IOP in Brimonidine group was not significant.

The rise in IOP 1 hour after the procedure was statistically significant in both the Topical Timolol and Brimonidine group. The rise in IOP was transient and continued to be high 4 hours after the procedure. The IOP normalised on the 3rd and 7th day of treatment. It was found out that the patients treated in the Timolol group had a mean rise in IOP of 4.18 mm Hg 1 hour after the procedure while the patients in th Brimonidine group had a mean rise of 3.32mm Hg 1 hour after the procedure. The chi- square test showed the p= 0.016 which was statistically very significant. Hence our study concludes that Brimonidine controls the transient rise in IOP better than Timolol following ND YAG Capsulotomy.

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