



Original Research Article

Evaluation of binocular once only instillation of timolol maleate 0.5% eye drop for treatment of presbyopia

Parthasarathi Roy^{1*}, Sanjukta Kar¹¹Dept. of Ophthalmology, Calcutta National Medical College, Kolkata, West bengal, India

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ABSTRACT

Introduction: When beta 2 mediated relaxing effect on ciliary muscle is blocked by Timolol maleate 0.5% eye drop, then there is increase of tonic accommodation, thus presbyopia is corrected. Therefore purpose of this placebo controlled trial is to determine and compare the near point of accommodation and amplitude of accommodation of the subjects before and after instillation of Timolol maleate 0.5% eye drop.

Materials and Methods: After getting approval from the Institutional ethics committee, and informed consent, we recruited 40 emmetropic subjects (80 eyes) of ages between 35-45 years, and randomly assigned them to binocular once only instillation of one drop of Timolol maleate 0.5% eye drop (intervention group, 20 subjects) or Normal saline eye drop (Control group, 20 subjects). Near points of Accommodation (NPA) were measured in these 40 subjects by RAF rule prior to giving eye drop and then at half hourly interval after instillation till effect started to wean off.

Statistical analysis: The statistical software SPSS version 25 was used for the analysis.

Study design: Prospective, assessor masked, randomised controlled interventional study.

Results: We found that the effect on NPA started to wean off after 8 hrs. However after an initial steady fall between 1-4 hr, NPA maintained a steady state between 4-8 hrs of instillation at points closer to eye by an average of 5.79 +/- 2.87cm (P < 0.001). This tantamounts to presbyopia correction of + 1.21 +/- 0.42 Dioptre (P < 0.001) sustained for 4 hrs between 4hrs and 8 hrs after instillation of drop.

Conclusion: One drop of Timolol maleate 0.5% eye drop instilled binocularly can achieve correction of presbyopia to the tune of + 1.21 +/- 0.42 Dioptre, sustained for 4 hrs between 4 and 8 hrs after instillation.

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1. Introduction

Presbyopia is an age-related condition where near point of eye recedes beyond the ordinary reading or working distance. In emmetropes it usually starts at around 40 years of age. Common treatments of presbyopia consist of use of reading glasses or bifocal/ multifocal eye glasses. Corrective contact lenses may also be used for correcting presbyopia. Surgical options are also available for correcting presbyopia, including eye surgery. Refractive surgery generally involves reshaping of cornea. Refractive surgery to one eye for near vision while leaving the

other eye for distant vision, is one of the modalities that may be employed. Intraocular lens implantation is another surgical option. However, eye glasses may be cosmetically unacceptable, lenses may be cumbersome or provide inadequate treatment, and surgery may be risky. In recent times there has been interest among researchers to develop pharmacological agents to treat presbyopia.¹ Karanfil FC et al (2017)² in their review article discussed the name, content and mechanism of action of these eye drops. Till date about fourteen commercial and non-commercial drops were used or tried in the treatment of presbyopia.²⁻¹⁹ Although the success to this aim is not overwhelming, some pharmacological agents have already

* Corresponding author.

E-mail address: ps_roy2002@yahoo.com (P. Roy).

been approved by U.S. Food and Drug administration.²⁰ However, some other drug which has potential for use in the treatment for presbyopia has not been evaluated till date. One such drug is Timolol maleate 0.5% eye drop which is commonly used as an intraocular pressure lowering agent in glaucoma for decades. Long-term evaluation of this drop was investigated in a study for a mean follow-up of 31.6 months in a group of 155 patients (275 eyes) with glaucoma or ocular hypertension, and found to be quite safe, serious side-effect requiring discontinuation was only 1.9%.²¹ In a resting state, the tone of the ciliary muscle is maintained by mutually opposite interaction between parasympathetic innervation through M3 receptor and sympathetic innervation through beta 2 adrenoceptor receptors. The parasympathetic innervation tends to contract the ciliary muscle and sympathetic innervation tends to relax the ciliary muscle. Therefore, blocking the sympathetic innervation by instilling beta blocker drug like Timolol maleate 0.5% eye drop will increase the tonic accommodation²² (as accommodation is caused by contraction of ciliary muscle) and therefore may be helpful in treatment of presbyopia. This mechanism spares pupillary muscles thus do not have any effect on pupillary diameter and also avoids side-effects of multi-drug combination drops which are currently under investigation. Correction of presbyopia by this mechanism of action of Timolol maleate 0.5% eye drop was evaluated for the first time in literature by our present study.

Hypotheses on Expected Outcome: Reduction of Near Point of Accommodation and increase of Amplitude of Accommodation are the two desirable outcomes of the study, which would be achieved by increase in tonic accommodation by unique mechanism of action of Timolol maleate 0.5% eye drop as described above. We also hypothesized that the undesirable side effects that accompany Pilocarpine eye drop, like reduction of distant acuity and reduction of intraocular pressure, would not apply to Timolol maleate 0.5% eye drop in our study. This is because of the fact that relieved of relaxing effect on it, excursion of ciliary muscle will be more, covering entire range of accommodation required for distant to near back and forth, thus bringing entire accommodation under facultative control of the individual. Our study would employ once-only one-drop Timolol maleate 0.5%, therefore reduction of intraocular pressure is unlikely to occur in this short term use.

2. Materials and Methods

2.1. Inclusion criteria

1. Informed consent by the participants.
2. Emmetropic subjects between 35-45 years age group with distant visual acuity 6/6 with no systemic or ocular pathology.

3. Intraocular pressure (IOP) 12 - 21 mm of Hg.
4. The patients included in the study did not receive any chronic mydriatic/miotic therapy previously.

2.2. Exclusion criteria

1. Age less than 35 and more than 45yrs.
2. Subjects with previous systemic or ocular pathology.
3. IOP less than 12 and more than 21 mm of Hg.
4. Patients who did not give informed consent prior to the study.
5. Subjects with history of ischemic heart disease.
6. Subjects with diabetes on insulin medication.
7. Subjects with history of depression.
8. Subjects with peripheral vascular disease.

Safety parameters of Timolol In our study. Before giving the eye drop 0.5% Timolol maleate, the history regarding the following were taken. 1. Asthma 2. History of bradycardia 3. Chronic Obstructive Pulmonary Disease (COPD) 4. Heart block 5. Allergic reaction (example - anaphylaxis, atopy) 6. Blood vessel disease 7. Myasthenia gravis 8. Lung disease 9. Diabetes 10. Glaucoma 11. Stage IV heart failure

After getting approval from the Institutional ethics committee, and informed consent, we recruited 40 emmetropic subjects (80 eyes) between 35-45 years age, and randomly assigned them to binocular once only instillation of one drop of Timolol maleate 0.5% eye drop (intervention group, 20 subjects) or Normal saline eye drop (Control group, 20 subjects). For every subject, Distant Visual Acuity, Intraocular pressure, Near Point of Accommodation measured by Royal Air Force Rule, were assessed prior to giving eye drop and then at 1/2 hr, 1 hr, 1 1/2 hrs, 2 hrs, 2 1/2 hrs, 3 hrs, 3 1/2 hrs, 4 hrs, 4 1/2 hrs, 5 hrs, 5 1/2 hrs, 6 hrs and if the effect does not wean off after 6 hrs half hourly examination to be continued till effect started to wean off. We found effect started to wean off after 8 hrs. In control group (Normal Saline eye drop) same measurements were taken. Amplitude of Accommodation was calculated for each NPA value by applying formula as below and included in the data analysis. Formula: $A = P - R$.

A = Amplitude of Accommodation; **P** = Refractive power (Dioptre) of eye at NPA=100/NPA;

R= Refractive power (Dioptre) of eye when looking at distance (∞)* = $100/\infty=0$

*As study subjects are emmetropic.

2.3. Statistical analysis

Continuous variables were expressed as Mean, Median and Standard Deviation and compared across the groups by Mann-Whitney U test since the data did not follow normal distribution as checked using Shapiro Wilk Test. The statistical software SPSS version 25 was used for the analysis. An alpha level of 5% has been taken, i.e. if any p value is less than 0.05 it has been considered as significant.

3. Results

The intervention and control groups were age and sex matched. The minimum and maximum age in intervention group were 35 years 42 years respectively, and in control group 36 years 44 years respectively. The mean age in intervention and control group were 37.3 \pm 2.31 years and 38.45 \pm 2.11 years respectively ($P = 0.1085$). Gender distribution in intervention group was Male: Female = 11(55%): 9(45%) and in control group 15 (75%): 5(25%) ($P= 0.185$). Hour-wise change of Near Point of Accommodation (in centimetre) and Amplitude of Accommodation (in Dioptre) in the Intervention and Control groups are shown in the Tables 1 and 2 respectively.

Graphical representations of hour-wise changes of Near Point of Accommodation are depicted; individual tracings of intervention group in Figure 1, that of control group in Figure 2 and comparison between intervention and control groups in Figure 3.

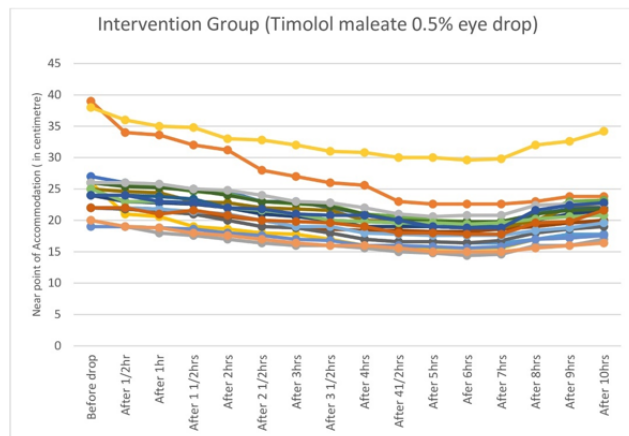


Figure 1: Graph showing individual tracings of NPA of twenty subjects in the intervention group: steady downward slope of NPA tracings soon after instillation of Timolol maleate 0.5% eye drop till four hours, followed by straightening between four to eight hours.

Similarly, graphical representations of hour-wise changes of Amplitude of Accommodation are also depicted in Figures 4, 5 and 6.

Near point of Accommodation started to come closer and closer to eye steadily and statistically significantly two hours after instillation of Timolol maleate 0.5% eye drop till four hours after drop, then remained almost stationary between four and eight hours, then the effect started to wean off. (Table 1, Figures 1, 2 and 3) Therefore Near point of Accommodation maintained a steady state between 4 and 8 hrs of instillation, at points closer to eye by an average 5.79 \pm 2.87cm ($P < 0.001$). (Table 1) This tantamounts to increase of amplitude of accommodation and thus to, presbyopia correction of + 1.21 \pm 0.42 Dioptre ($P < 0.001$) sustained for 4 hrs between 4hrs and 8 hrs after instillation

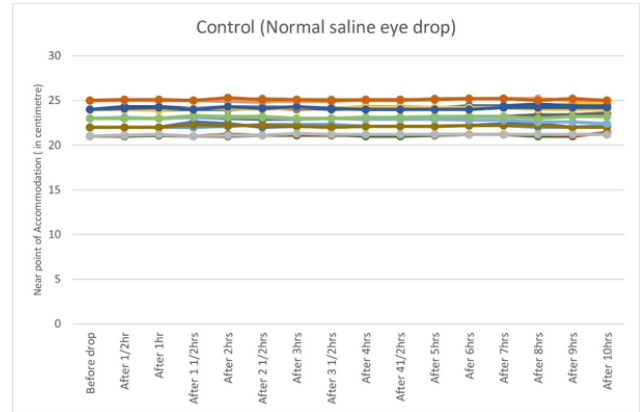


Figure 2: Graph showing normal saline eye drop (Placebo) had no effect on NPA .

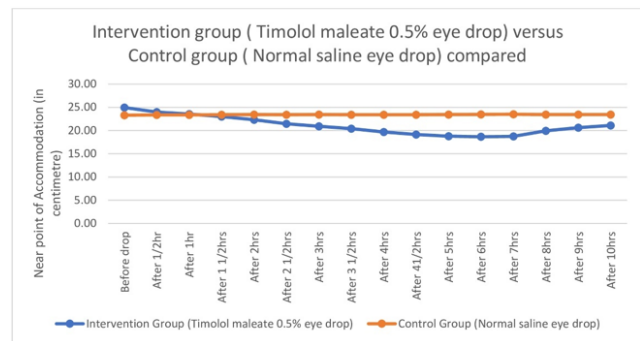


Figure 3: Graph showing comparison of Near Point of Accommodation between Intervention (Timolol maleate 0.5% eye drop) and Control group (Normal saline eye drop).

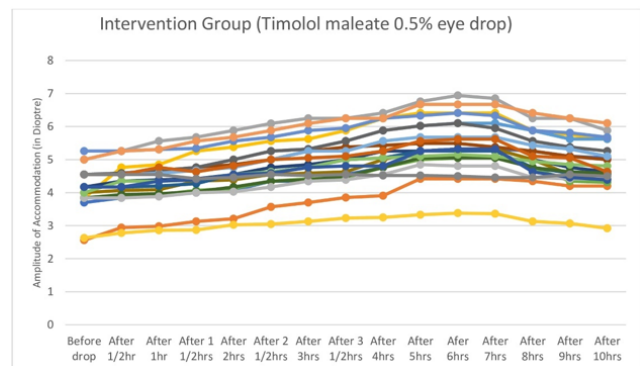


Figure 4: Graph showing steady upward slope of amplitude of accommodation soon after instillation of timolol maleate 0.5% eye drop till four hours, followed by flattening between four and eight hours.

Table 1: Hour-wise change of Near Point of Accommodation (in centimetre)

Near point of accommodation (Centimetre)	Group Intervention			Control			p Value	Significance
	Mean	Median	Std. Deviation	Mean	Median	Std. Deviation		
before drop	24.95	24.00	5.17	23.30	24.00	1.38	0.323	Not Significant
After 1/2hr	23.96	23.00	4.38	23.35	24.00	1.39	0.828	Not Significant
After 1hr	23.56	22.90	4.33	23.35	23.95	1.37	0.551	Not Significant
After 1 1/2hrs	23.00	22.70	4.23	23.39	24.00	1.35	0.183	Not Significant
After 2hrs	22.31	22.00	4.05	23.44	24.05	1.37	0.018	Significant
After 2 1/2hrs	21.44	21.30	3.81	23.40	24.05	1.36	0.002	Significant
After 3hrs	20.92	20.80	3.72	23.42	24.05	1.36	0.001	Significant
After 3 1/2hrs	20.39	20.00	3.57	23.38	24.00	1.35	<0.001	Significant
After 4hrs	19.69	19.40	3.61	23.39	24.00	1.38	<0.001	Significant
After 4 1/2hrs	19.14	19.30	3.34	23.39	24.00	1.38	<0.001	Significant
After 5hrs	18.79	19.00	3.31	23.42	24.05	1.38	<0.001	Significant
After 6hrs	18.66	18.80	3.29	23.48	24.05	1.39	<0.001	Significant
After 7hrs	18.73	18.80	3.29	23.50	24.20	1.38	<0.001	Significant
After 8hrs	19.94	19.80	3.52	23.45	24.00	1.43	<0.001	Significant
After 9hrs	20.61	20.20	3.65	23.43	24.00	1.42	<0.001	Significant
After 10hrs	21.10	21.20	3.80	23.45	24.00	1.35	<0.001	Significant
Change After 1/2hr	0.99	0.40	1.51	-0.05	0.00	0.08	<0.001	Significant
Change After 1hr	1.39	0.90	1.55	-0.05	0.00	0.09	<0.001	Significant
Change After 1 1/2hrs	1.95	1.30	1.87	-0.09	0.00	0.15	<0.001	Significant
Change After 2hrs	2.64	2.00	1.91	-0.14	-0.10	0.13	<0.001	Significant
Change After 2 1/2hrs	3.51	3.00	2.27	-0.10	-0.10	0.13	<0.001	Significant
Change After 3hrs	4.03	3.20	2.31	-0.12	-0.10	0.13	<0.001	Significant
Change After 3 1/2hrs	4.56	4.00	2.51	-0.08	-0.10	0.10	<0.001	Significant
Change After 4hrs	5.26	5.00	2.48	-0.09	-0.10	0.09	<0.001	Significant
Change After 4 1/2hrs	5.81	5.10	2.89	-0.09	-0.10	0.09	<0.001	Significant
Change After 5hrs	6.16	5.40	2.91	-0.12	-0.10	0.08	<0.001	Significant
Change - After 6hrs	6.29	5.60	2.89	-0.17	-0.20	0.11	<0.001	Significant
Change - After 7hrs	6.22	5.30	2.92	-0.20	-0.20	0.11	<0.001	Significant
Change - After 8hrs	5.01	4.20	3.12	-0.15	-0.20	0.21	<0.001	Significant
Change - After 9hrs	4.34	3.40	3.10	-0.13	-0.10	0.22	<0.001	Significant
Change - After 10hrs	3.85	3.00	3.25	-0.15	-0.20	0.26	<0.001	Significant

of drop.(Table 2, Figures 4, 5 and 6)

There was no statistically significant fall of intraocular pressure (Table 3, Figure 7) or reduction of distant VA (Figure 8). In the intervention group intraocular pressure never fell below 12 mm of Hg, Distant VA never fell below 6/6 (i.e. pre-drop value)

4. Discussion

In November 2021, U.S. FDA has approved 1.25% Pilocarpine hydrochloride eye drop for treating presbyopia. This is the only U.S. FDA approved eye drop for presbyopia till date.²⁰ Pilocarpine causes constriction of pupil and thus causes miosis related side effects like constriction of visual field etc. Roy P et al was first to exploit capsule slackening effect of Timolol maleate 0.5% eye

drop by the mechanism of increased tonic accommodation in hypermature intumescent cataract surgery.²³ Correction of presbyopia as done in our study by this mechanism of action of Timolol maleate 0.5% eye drop, has not been explored and evaluated before. This mechanism spares pupillary muscles thus does not have any effect on pupillary diameter and also avoids side-effects of multi-drug combination drops which are currently under investigation. The advancing Near Point of Accommodation towards eye and corresponding increase of Amplitude of Accommodation were on expected line as hypothesised. Moreover relieved of relaxing effect on it, excursion of ciliary muscle is now more, covering entire range of accommodation requiring for distant and near vision, thus bringing entire accommodation under facultative control of

Table 2: Hour-wise change of Amplitude of Accommodation (in Dioptre)

Amplitude of accommodation (Dioptre)	Group						p Value	Significance
	Mean	Intervention Median	Std. Deviation	Mean	Control Median	Std. Deviation		
Before drop	4.14	4.17	0.69	4.31	4.17	0.26	0.323	Not Significant
After 1/2hr	4.29	4.35	0.66	4.30	4.17	0.26	0.828	Not Significant
After 1hr	4.36	4.37	0.69	4.30	4.18	0.26	0.551	Not Significant
After 1 1/2hrs	4.47	4.41	0.71	4.29	4.17	0.26	0.183	Not Significant
After 2hrs	4.61	4.55	0.73	4.28	4.16	0.26	0.018	Significant
After 2 1/2hrs	4.79	4.70	0.74	4.29	4.16	0.26	0.002	Significant
After 3hrs	4.91	4.81	0.77	4.28	4.16	0.25	0.001	Significant
After 3 1/2hrs	5.03	5.00	0.77	4.29	4.17	0.26	<0.001	Significant
After 4hrs	5.22	5.16	0.81	4.29	4.17	0.26	<0.001	Significant
After 5hrs	5.45	5.26	0.80	4.28	4.16	0.26	<0.001	Significant
After 6hrs	5.49	5.32	0.82	4.27	4.16	0.26	<0.001	Significant
After 7hrs	5.47	5.32	0.80	4.27	4.13	0.26	<0.001	Significant
After 8hrs	5.14	5.05	0.75	4.28	4.17	0.27	<0.001	Significant
After 9hrs	4.98	4.95	0.76	4.28	4.17	0.27	<0.001	Significant
After 10hrs	4.86	4.72	0.73	4.28	4.17	0.25	<0.001	Significant
Change After - 1/2hr	0.15	0.07	0.22	-0.01	-0.00	0.01	<0.001	Significant
Change After - 1hr	0.22	0.16	0.23	-0.01	-0.00	0.02	<0.001	Significant
Change After - 1 1/2hrs	0.33	0.23	0.31	-0.02	-0.00	0.03	<0.001	Significant
Change After - 2hrs	0.47	0.38	0.30	-0.03	-0.03	0.03	<0.001	Significant
Change After - 2 1/2hrs	0.65	0.53	0.32	-0.02	-0.02	0.02	<0.001	Significant
Change After - After 3hrs	0.77	0.67	0.32	-0.02	-0.03	0.03	<0.001	Significant
Change After - 3 1/2hrs	0.89	0.83	0.36	-0.02	-0.02	0.02	<0.001	Significant
Change After - 4hrs	1.08	1.01	0.39	-0.02	-0.02	0.02	<0.001	Significant
Change After - 5hrs	1.31	1.15	0.42	-0.02	-0.02	0.02	<0.001	Significant
Change - After 6hrs	1.35	1.18	0.42	-0.03	-0.04	0.02	<0.001	Significant
Change - After 7hrs	1.33	1.18	0.43	-0.04	-0.04	0.02	<0.001	Significant
Change - After 8hrs	1.00	0.92	0.44	-0.03	-0.03	0.04	<0.001	Significant
Change - After 9hrs	0.84	0.68	0.44	-0.02	-0.01	0.04	<0.001	Significant
Change - After 10hrs	0.72	0.57	0.46	-0.03	-0.04	0.05	<0.001	Significant

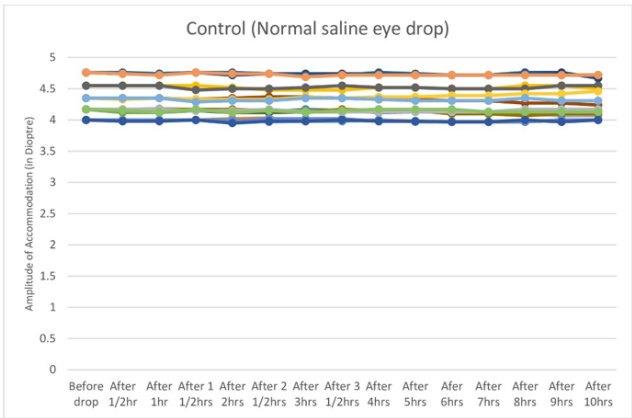


Figure 5: Graph showing normal saline eye drop (Placebo) had no effect on amplitude of accommodation.

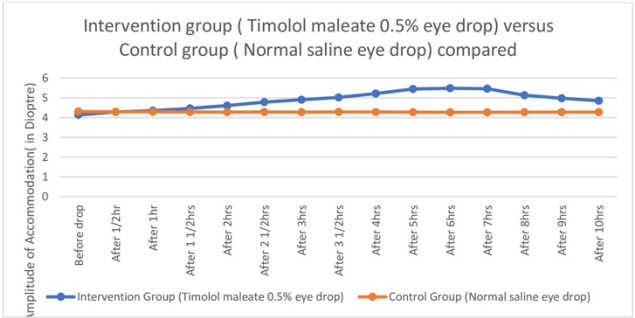
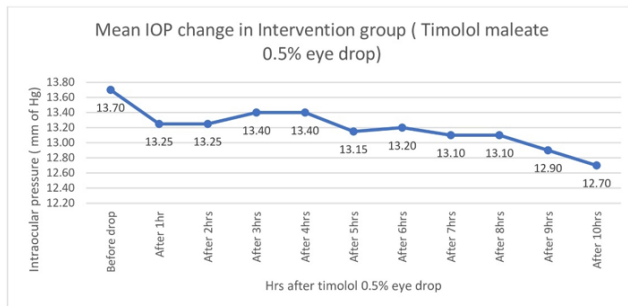
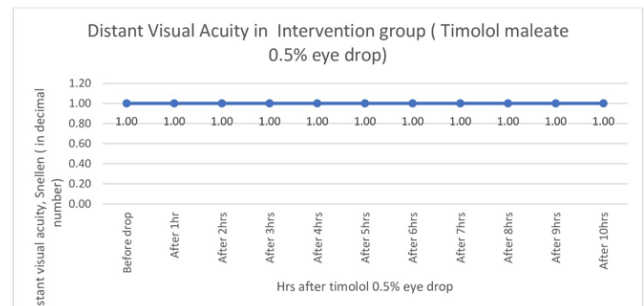


Figure 6: Graph showing comparison of Amplitude of accommodation between Intervention (Timolol maleate 0.5% eye drop) and Control group (Normal saline eye drop)

the individual. Therefore another benefit of exploiting this mechanism lies in that there is no blurring of distant vision

Table 3: Hourly change of intraocular pressure in Intervention group (Timolol maleate 0.5% eye drop) and Control group (Normal saline eye drop)

IOP in mm of Hg	Intervention			Control			p Value	Significance
	Mean	Median	Std. Deviation	Mean	Median	Std. Deviation		
before giving eye drop	13.70	14.00	1.81	13.65	14.00	1.84	0.921	Not Significant
IOP after 1hr of giving drop	13.25	14.00	2.02	13.60	14.00	1.76	0.661	Not Significant
IOP after 2hrs	13.25	14.00	1.55	13.60	14.00	1.76	0.574	Not Significant
IOP after 3hrs	13.40	14.00	1.31	13.60	14.00	1.76	0.705	Not Significant
IOP after 4hrs	13.40	14.00	1.31	13.60	14.00	1.76	0.705	Not Significant
IOP after 5hrs	13.15	14.00	1.27	13.55	14.00	1.70	0.542	Not Significant
IOP after 6hrs	13.20	14.00	1.01	13.65	14.00	1.63	0.471	Not Significant
IOP after 7hrs	13.10	14.00	1.02	13.40	14.00	1.47	0.618	Not Significant
IOP after 8hrs	13.10	14.00	1.02	13.40	14.00	1.47	0.618	Not Significant
IOP after 9hrs	12.90	12.00	1.21	13.40	14.00	1.47	0.270	Not Significant
IOP after 10hrs	12.70	12.00	0.98	13.10	13.00	1.21	0.294	Not Significant
Change after 1hr	0.45	0.00	1.05	0.05	0.00	0.22	0.054	Not Significant
Change after 2hrs	0.45	0.00	0.94	0.05	0.00	0.22	0.074	Not Significant
Change after 3hrs	0.30	0.00	1.42	0.05	0.00	0.22	0.403	Not Significant
Change after 4hrs	0.30	0.00	1.42	0.05	0.00	0.22	0.403	Not Significant
Change after 5hrs	0.55	0.00	1.43	0.10	0.00	0.55	0.192	Not Significant
Change after 6hrs	0.50	0.00	1.57	0.00	0.00	0.73	0.232	Not Significant
Change after 7hrs	0.60	0.00	1.60	0.25	0.00	0.97	0.390	Not Significant
Change after 8hrs	0.60	0.00	1.60	0.25	0.00	0.97	0.390	Not Significant
Change after 9hrs	0.80	0.00	2.04	0.25	0.00	0.97	0.258	Not Significant
Change after 10hrs	1.00	0.50	1.78	0.55	0.00	1.32	0.318	Not Significant

**Figure 7:** Graph showing change of mean IOP after instillation of Timolol maleate 0.5% eye drop**Figure 8:** Graph showing timolol maleate 0.5% eye drop had no effect on distant visual acuity.

as was hypothesized in the beginning of the study. Also as hypothesized there was no statistically significant fall of intraocular pressure.

5. Conclusion

Binocular once only instillation of one drop of Timolol maleate 0.5% eye drop showed promise for use in the treatment of presbyopia in 35-45 years age group, by adding + 1.2 Dioptre power to refractive system of eye. There was no blurring of distant vision and no significant fall of intraocular pressure. Findings of this research may

be utilised for short term near work involving household work like cooking, stitching and office work like lectures, seminars, meetings etc. Future research lies on increasing the duration of action exceeding 4 hrs by instillation of top-up drop.

6. Conflict of Interest

None.

7. Source of Funding

None.

References

- Grzybowski A, Ruamviboonsuk V. Pharmacological Treatment in Presbyopia. *J Clin Med*. 2022;11(5):1385. doi:10.3390/jcm11051385.
- Karanfil FÇ, Turgut B. Update on Presbyopia-correcting Drops. *Eur Ophthalmic Rev*. 2017;11(2):99–102.
- Benozzi J, Benozzi G, Orman B. Presbyopia: a new potential pharmacological treatment. *Med Hypothesis Discov Innov Ophthalmol*. 2012;1(1):3–5.
- Patel S, Salamun F, Matovic K. Pharmacological treatments of presbyopia: a review of modern perspectives. *Eye Vis (Lond)*. 2013;4:3. doi:10.1186/s40662-017-0068-8.
- Kaufman S. Addressing presbyopia pharmacologically. *Ophthalmology Times*; 2012. (Accessed 13th February, 2024). Available from: <https://www.opthalmologytimes.com/view/addressing-presbyopia-pharmacologically>.
- Abdelkader A. Improved presbyopic vision with miotics. *Eye Contact Lens*. 2015;41(5):323–7.
- Vejarano LF. Ophthalmic formulation and method for ameliorating presbyopia, 2012. Patent publication number: US20140024642 A1; 2012. (Accessed 13th February, 2024). Available from: <http://bit.ly/Vejarano>.
- Krader CG, Feinbaum C. Simple solution for presbyopia: topical agent acts by reducing pupil size to increase depth of focus. *Ophthalmology Times*; 2015. (Accessed 13th February, 2024). Available from: <https://www.opthalmologytimes.com/view/simple-solution-presbyopia>.
- Rodríguez HJV, Carrera DH. Composición oftálmica para la corrección de la presbicia ,2014,. Patent publication number: WO2015092087A1; 2014. (Accessed 13th February, 2024). Available from: <http://bit.ly/Rodríguez>.
- Renna A, Alió JL, Vejarano LF. Pharmacological treatments of presbyopia: a review of modern perspectives. *Eye Vis (Lond)*. 2017;4:3. doi:10.1186/s40662-017-0068-8.
- Balal S, Gil-Cazorla R, Naroo SA, Sharma A, Shah S. Eyedrops for presbyopia. Myth or medicine? *Ophthalmologist*. 2017;37:16–27.
- German EJ, Wood D, Hurst MA. Ocular effects of antimuscarinic compounds: is clinical effect determined by binding affinity for muscarinic receptors or melanin pigment? *J Ocul Pharmacol Ther*. 1999;15(3):257–69.
- Moustafa FA, Sandoval LF, Feldman SR. Rosacea: new and emerging treatments. *Drugs*. 2014;74(13):1457–65.
- Allergan, A study of the concurrent use of AGN-190584 and AGN-199201 in participants with presbyopia. ClinicalTrials.gov Identifier: NCT02595528; 2016. (Accessed on 13th February, 2024). Available from: <http://bit.ly/NCT02595528>.
- Crawford KS, Garner WH, Burns W. Dioptin™: A novel pharmaceutical formulation for restoration of accommodation in presbyopes. *Invest Ophthalmol Vis Sci*. 2014;55:3765.
- Takemoto L. Increase in the intramolecular disulfide bonding of alpha-a crystallin during aging of the human lens. *Exp Eye Res*. 1996;63(5):585–90.
- Encorehealth L, Esters C. 2014. Available from: [http://bit.ly/cholineesters\(accessedon13th](http://bit.ly/cholineesters(accessedon13th).
- Burns B. Encore Vision Reports Positive Phase I/II Results; 2016. (Accessed on 13th February, 2024). Available from: [http://bit.ly/EV06presbyopia\(accessedon13th](http://bit.ly/EV06presbyopia(accessedon13th).
- Novartis AG. Novartis bolsters ophthalmology pipeline though the acquisition of Encore Vision, Inc; 2016. (Accessed on 13th February, 2024). Available from: <http://bit.ly/encorenovartis>.
- Harrison L. FDA Approves Eye Drops for Presbyopia ; 2024. [Accessed on 31st January, 2024] . Available from: <https://www.medscape.com/viewarticle/961999#vp2>.
- Uusitalo RJ, Palkama A. Long-term evaluation of timolol. *Acta Ophthalmol (Copenh)*. 1989;67(5):573–81.
- Winn B, Culhane HM, Gilmartin B, Strang NC. Effect of beta-adrenoceptor antagonists on autonomic control of ciliary smooth muscle. *Ophthalmic Physiol Opt*. 2002;22(5):359–65.
- Roy P, Ganguli S, Tripathi SK. Pre-operative minimal-cycloplegia mydriasis for capsulorhexis in hypermature intumescent cataract. *Ind J Clin Exp Ophthalmol*. 2023;9(2):193–8.

Author's biography

Parthasarathi Roy, Associate Professor

Sanjukta Kar, Junior Resident

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