International Journal of Medical Research Professionals
P-ISSN: 2454-6356; E-ISSN: 2454-6364
DOI: 10.21276/ijmrp

IJMRP

Original Research Article.

Effect on Ciliary Muscles and Accommodation: Comparative Study Between Topical Tropicamide 1% versus Combination of Tropicamide 0.8% and Phenylephrine 5%

Sedhu P.A[1], Archana Pushpakaran[2*], Cyriac Kurian[3]

[1]Associate Professor, [2*]Assistant Professor, [3]Professor & Head, Department of Ophthalmology, Sree Narayana Institute of Medical Sciences, Chalakka, Ernakulam, Kerala, India.

ABSTRACT

Background: Cycloplegia is the paralysis of the ciliary muscles achieved by blocking the muscarinic receptors normally stimulated by the release of acetylcholine from the nerve endings of the parasympathetic system. The study is done to compare effect of 1% tropicamide solution with a combination of 0.8% tropicamide and 5% phenylephrine, for the degree of cycloplegia and the amount of residual accommodation at 20 minutes after instillation of the drop.

Methods: In this prospective, randomized study, 150 patients who presented to the Department of Ophthalmology were evaluated for cycloplegia. They received 1 drop of Tropicamide 1% in one eye and the combination drop in the other eye. The cycloplegia and residual accommodation were assessed at 20 minutes using the autorefractometer.

Results: In the eyes that received Tropicamide 1%, the mean cycloplegia measured at 20 minutes was 1.12 D and the mean residual accommodation was 1.20 D. In the eyes that received the combination drop, the mean cycloplegia was 1.05 D and the mean residual accommodation was 1.26 D. Though the cycloplegic effect of tropicamide 1% was marginally better than the combination drop, the difference in the two groups was not statistically significant for cycloplegia (p=0.007) or residual accommodation (p=0.15).

Conclusion: A single drop of a combination of 0.8% tropicamide and 5% phenylephrine achieves adequate cycloplegia, in patient 11- 40 years of age.

Keywords: Cycloplegia; Tropicamide; Phenylephrine.

***Correspondence to:**

Dr. Archana Pushpakaran,
Assistant Professor, Dept.of Ophthalmology
Sree Narayana Institute of Medical Sciences,
Chalakka, Ernakulam, Kerala, India.

Article History:

Received: 19-08-2017, **Revised:** 13-09-2017, **Accepted:** 28-09-2017

Access this article online	
Website: www.ijmrp.com	Quick Response code
DOI: 10.21276/ijmrp.2017.3.5.064	

INTRODUCTION

Cycloplegia is the paralysis of the ciliary muscles achieved by blocking the muscarinic receptors normally stimulated by the release of acetylcholine from the nerve endings of the parasympathetic system. Since the parasympathetic nervous system also enervates the pupil sphincter pupillae muscle, cycloplegia is always accompanied by mydriasis (although mydriasis is not always accompanied by cycloplegia. Cycloplegic drugs are used to produce the above effects and can thus prevent or reduce accommodation during refraction, thus making latent refractive errors manifest.[1,2]

A proper and adequate fundoscopic examination is central to accurate diagnosis and treatment in the practice of optometry. A satisfactory prescription for glasses may be given only after the examiner has accurately determined the refractive status of the eye and made allowances for the tonus of the ciliary body or the accommodative power. In ophthalmic practice, mydriatics and cycloplegics are required on a regular basis for refraction and fundus evaluation. Cycloplegics inhibit accommodation and allow latent refractive errors to become manifest, thus enabling an accurate estimation of the error. A well dilated pupil helps the refraction to be carried out more easily and accurately, and also allows a thorough examination of the lens and fundus.[3-7]

The cycloplegic agents used are atropine, cyclopentolate and tropicamide. Whereas atropine and cyclopentolate are effective in children, they have a much longer duration of action than tropicamide, and are less effective for rapid mydriasis. Tropicamide produces rapid mydriasis and adequate cycloplegia in adults, but it is not known if it is an effective cycloplegic agent in children, who have a higher ciliary muscle tone. Cycloplegic agents are drugs that act by antagonizing the muscarinic action of acetylcholine. They do so by blocking its action at structures innervated by postganglionic parasympathetic nerve fibres. These agents paralyse the constrictor pupillae as well as the ciliary muscle, causing mydriasis as well as cycloplegia. For many years, atropine was the only cycloplegic agent available. To bring about full cycloplegia in children, it had to be instilled two or three times

daily for three days prior to cycloplegic refraction. The resulting cycloplegia persisted for seven to ten days and the accompanying mydriasis lasted as long as two weeks.[8-12]

The sphincter pupillae and ciliary muscles, which belong to the adrenergic system, are innervated by the postganglionic parasympathetic efferent fibres of the short ciliary nerve branches of the occulomotor nerve (CN III) that have synapsed in ciliary ganglion. The dilator pupillae muscle is innervated by long ciliary nerves carrying postganglionic fibres of the sympathetic nervous system that have synapsed in the superior cervical ganglion. Cholinergic stimulation of the sphincter pupillae muscle causes papillary constriction (miosis), and cholinergic stimulation of the ciliary muscle brings about increased accommodation. Blockade of the cholinergic system dilates the pupil (mydriasis) and relaxes the ciliary muscle, causing a decrease in accommodation (cycloplegia).[13-17]

The aim of our study was to compare I% tropicamide solution with a combination of 0.8% tropicamide and 5% phenylephrine, for cycloplegia. The objective of our study was to evaluate the degree of cycloplegia and the amount of residual accommodation at 20 minutes after instillation of the drop.

MATERIALS AND METHODS

A prospective & randomized study was done in Department of Ophthalmology on 150 patients who were evaluated for cycloplegia in OPD.

Exclusion Criteria

1. Patients already using mydriatics or cycloplegics.
2. All cases of glaucoma.
3. Patients with Best Corrected Visual Acuity < 6/60 or near vision <N12, to exclude patients with poor vision who would not be able to perform the tests.
4. Post ocular surgery.
5. Hypertensive patients.
6. Diabetic patients as they are known to have rigid pupils which are more difficult to dilate.
7. Patients on systemic drugs that could affect the pupil or accommodation, e.g. psychotherapeutic drugs.
8. Patients suspected to have ciliary muscle spasm, resulting in artificially increased amount of myopia.
9. Patients with known pseudoexfoliation syndrome, in whom the pupils are expected to be rigid.

Proper history was taken and detailed examination was done. Patients were informed about the study and written consent was taken. Non cycloplegic refraction at baseline was estimated using the Automated Refractometer as follows: a) Patients were first presented with the distant target at 6m and the spherical equivalent for distance was noted. b) Then the near target at 33cm was present. The patients were asked to view the target and report it as seen clearly, if not, a near add was presented on the machine, which was within the target.

The post cycloplegic refraction was measured on the auto-refractometer at 20 minutes. The measurement was done in a similar manner to that described earlier, with the patients first being presented with the distant target and then the near target. The near add was increased till the patients were able to see the target clearly. Compared to the non cycloplegic refraction, post cycloplegia all the patients required an increased amount of near add to view the same target clearly.

The residual accommodation was measured as follows: the amount of plus add was increased till the target became clear, the plus add was further increased till the target appeared to blur. The difference in the maximum and minimum amount of plus power between which the patient could see the target clearly, gave the amount of residual accommodation remaining after cycloplegia.

For the purpose of analysis, the 300 eyes of 150 patients were divided into two groups of 150 each; Group T included eyes which received Tropicamide 1% and Group TP included eyes which received the fixed combination of 0.8% Tropicamide with 5% Phenylephrine. Further, to study the effect of age on the various parameters, the patients were divided into 3 groups; Group 1 included patients between 11 — 20 years of age, Group 2: 21 — 30 years and Group 3: 31 — 40 years.

To negate the effect of positive and negative values of spherical equivalent recorded at baseline and at 20 minutes, the difference in the 2 readings of spherical equivalent was taken for statistical analysis, to study the latent error uncovered by the two drugs. Cycloplegia was calculated as the differences in the amounts of near add required to view the near target before and after instillation of drops. All other parameters evaluated were taken as quantitative data. All data were recorded in a proforma designed specifically for this study.

The data was analyzed as follows: first the descriptive statistics were computed. These included the range mean and standard deviation for quantitative variables, and category frequency counts and percentages for qualitative variables. Univariate analysis to evaluate correlation between 2 parameters was done using Student's t test and analysis of variance (ANOVA) was performed when there were more than two categories. To study the differences in the effect of the two drugs over the period of evaluation. Repeated Measures ANOVA (RMANOVA) was done. To evaluate any correlation between latent error, residual accommodation and cycloplegia, linear regression analysis was done. Statistical significance was considered when p w. < 0.05. All statistical analysis was done using SPSS Version 10.0 Statistical package.

RESULTS

In our study titled "Effect on Ciliary Muscles and Accommodation: Comparative Study between Topical Tropicamide 1% versus Combination of Tropicamide 0.8% and Phenylephrine 5%", a total of 150 Indian patients presenting for refraction or fundus evaluation were included. Two groups were studied — Group T being the eyes which received Tropicamide 1% and Group TP being the eyes which received the combination drop - Tropicamide 0.8% with Phenylephrine 5%. The 2 groups were compared for the cycloplegic effect, measured at 20 mins from baseline.

There was no statistically significant difference in the change in refraction readings (latent error) over time between the two groups (p=0.23) [Table 1].

There was a marginal difference in the near add between the two groups over time, with a higher near add required for group T, which was not statistically significant (p = 0.08). Cycloplegia induced by each group was further calculated by deducting the baseline near add from the 20 mins near add. The mean (± SD) cycloplegia for Group 1 was 1.12 (± 0.33) and for Group 2 was 1.05 (± 0.34); the difference was not statistically significant (p = 0.08) [Table 2].

Table 1: Changes in spherical equivalent over time.

Spherical equivalent	Mean (SD)	Statistical test
Baseline – Group 1	-0.64 (1.39)	F = 1.143
Baseline – Group 2	-0.66 (1.43)	P = 0.23
20 mins – Group 1	-0.44 (1.44)	
20 mins – Group 2	-0.40 (1.43)	

Table 2: Changes in near add over time (cycloplegia).

Near Add	Mean (SD)	Statistical test
Baseline – Group 1	0.25 (0.33)	F = 3.081
Baseline – Group 2	0.28 (0.35)	P = 0.08
20 mins – Group 1	1.37 (0.44)	
20 mins – Group 2	1.32 (0.43)	

Table 3: Residual accommodation.

Group	Mean	SD	t	df	P
T	1.20	0.36	1.45	298	0.15
TP	1.26	0.36			

Figure 1: Comparison of residual accommodation in two groups.

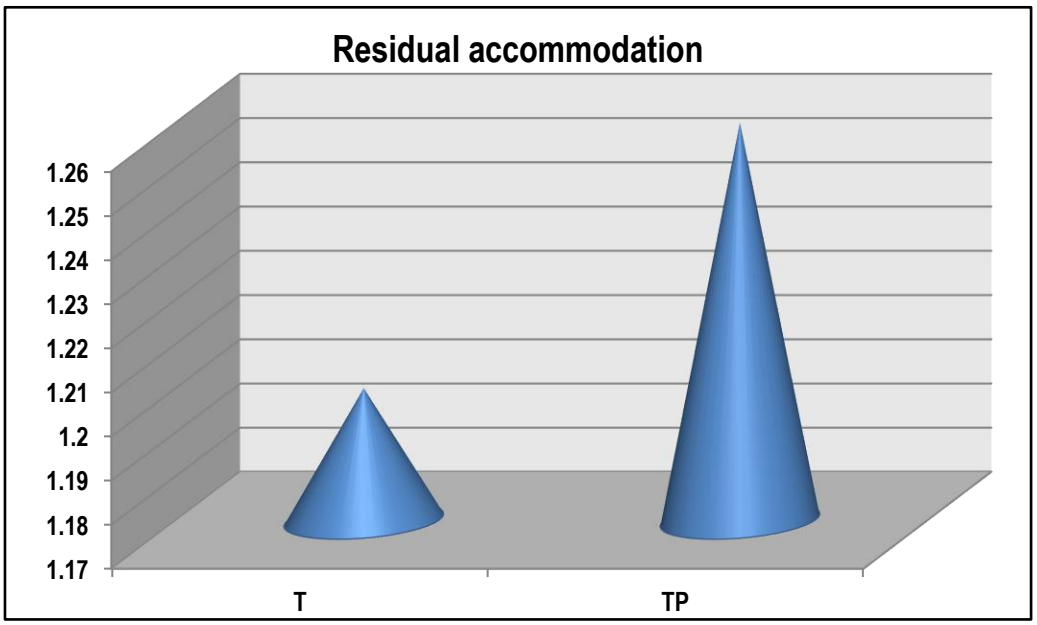

Table 4: Correlation b/w latent error and amount of cycloplegia and residual accommodation.

Parameter	Beta coefficient	t	P
Latent error vs Residual accommodation	0.06	1.04	0.30
Latent error vs Cycloplegia	0.32	0.55	0.57

Table 5: Effect of age on residual accommodation and cycloplegia.

Parameter	Age group	Mean (± SD)	F	df	P
Cycloplegia	**1**	0.95 (0.32)	18.25	2	<0.001
	2	1.19 (0.29)			
	3	1.14 (0.36)			
Residual	**1**	1.39 (0.38)	30.94	2	<0.001
Accommodation	**2**	1.19 (0.23)			
	3	1.0 (0.40)			

The measured residual accommodation in Group T was marginally lower than that in Group TP. however the difference was not statistically significant (p = 0.15) [Table 3, Figure 1].

There was no statistically significant co-relation between the latent error with either residual accommodation (p = 0.30) or cycloplegia (p = 0.57) [Table 4].

The near add at baseline and at 20 minutes increased with increasing age, the difference between the groups was statistically significant (p < 0.001). The amount of cycloplegia increased with increasing age, the difference between the age groups was statistically significant (p < 0.001). The residual accommodation decreased with increasing age, the difference was statistically significant (p < 0.001) [Table 5].

DISCUSSION

Accommodation is controlled by the action of the ciliary muscle, which is innervated by the autonomic nervous system (ANS). This system influences numerous ocular functions through parasympathetic and sympathetic innervations. The control of accommodation is mediated primarily by parasympathetic input, resulting in changes in the dioptric power of the crystalline lens. Nevertheless, there exists evidence supporting also a sympathetic innervation of ciliary muscle.[18,19]

A state of paralysis of the ciliary muscles is called cycloplegia. It may be produced by drugs instilled into the conjunctival sac, including atropine, homatropine, scopolamine, and tropicamide. These also paralyze the sphincter muscle of the iris causing a dilation of the pupil. For this reason, they are also called mydriatics. Most drugs which dilate the pupil also paralyse accommodation to some extent. Both these properties – cycloplegia and mydriasis – are utilized in the estimation of refractive errors. By paralysing the parasympathetic nerve supply, all accommodation for near sight can be abolished and refractive errors which before were latent are made manifest. The dilation of the pupil moreover makes the technique of estimating the error easier and helps to allow a thorough and easy examination of the interior of the eye.[20]

With a reduction in the strength of tropicamide in the fixed drug combination, the efficacy of the combination as a good cycloplegic was in doubt. This study has shown that the combination drug produced adequate cyclopegia after instillation of a single drop which was comparable to that induced by tropicamide alone.

The adequacy of a drug as a cycloplegic is evaluated by measuring the amount of residual accommodation remaining after its use. Our literature search did not reveal any method which would directly measure the amount of induced cycloplegia. The reports vary slightly on the acceptable amount of residual accommodation for adequate cycloplegia; most authors agree that less than 2 D of residual accommodation is acceptable.[4,8]

The earlier methods using the various near point rules (RAF rule, Prince rule etc) obtained a subjective assessment of the residual accommodation. Now with the availability of autorefractometers, this can be calculated objectively as the difference between the distance and near autorefraction.[18,20] In our study we attempted to calculate not only the residual accommodation but also the amount of cycloplegia caused. The calculations were made on the autorefractometer, using a combination of the subjective and objective method as per our machine parameters. After the distance autorefraction, the near target on the machine was presented, which stimulates accommodation. The difference in the amount of near add required to view the near target before and after using the drops, is suggested as a method of directly calculating the amount of cycloplegia caused by the drug. This method of calculating induced cycloplegia has not been reported by any other study to the best of our knowledge.

At baseline, the average near add required to view the target was 0.25 for the group receiving tropicamide and 0.28 the group receiving the combination drop, with no statistically significant difference in the two groups. Twenty minutes after instillation of the drops, the near add required to view the same target increased to a mean of 1.37 (±0.44) in group T and 1.32 (±0.43) in group TP, indicating a marginally higher add required by the group who received tropicamide 1% alone. However, this difference was not found to be statistically significant (p = 0.08). The mean cycloplegia measured at 20 minutes for Group T was 1.12 (± 0.33) and for Group TP was 1.05 (± 0.34) which was not statistically significant (p = 0.07).

The residual accommodation was calculated after the near add was given. The near add was increased till the subject reported blurring of the target. The difference between this value and the previous value gave the amount of residual accommodation. This is similar to the earlier subjective methods used, the difference being that we did it on the autorefractometer. By this method, the mean residual accommodation for the eyes receiving tropicamide 1% was 1.20 (± 0.36) D, and that for the eyes receiving the combination drop was 1.26 (± 0.36) D. The values were marginally lower in the 1st group, however this difference was not statistically significant (p = 0.15) with both groups well within the limits of 2 D of residual accommodation agreed upon by different authors. The lack of statistically significant difference in residual accommodation and induced cycloplegia between the 2 groups indicates that the combination drop which contains reduced amounts of tropicamide is as effective a cycloplegic as 1% tropicamide alone. Hence in clinical practice, the combination drug may be used as a single drop in situations requiring adequate mydriasis and cycloplegia together or in isolation.

After instillation of drops, there was a mean hypennetropic shift (latent error) in the refraction from baseline because of the induced cycloplegia. The latent error uncovered by the cycloplegia was 0.21 D in group T and 0.26 D in group TP. The amount of cycloplegia and residual accommodation should influence the estimation of refractive error. However, we did not find any correlation between latent error and cycloplegia or residual accommodation. Our result is similar to the study done by Manny et al (46). The significance of the above finding is not understood at the present time. On analysis by age groups, it was found that the residual accommodation was higher in the younger age groups compared to the older age groups: 1.39 (± 0.38) In group 1, 1.19 (±0.23) in Group 2 and 1.0 (± 0.40) in Group 3. The difference between the groups was statistically significant (p < 0.01) indicating that the drugs produces less cycloplegia in younger persons who are known to have a higher accommodative tone. However, in each group, the mean value for residual accommodation was less than 2 D, indicating that the cycloplegia was adequate for refraction. The amount of near add required at baseline was analyzed according to age groups, and it was found that Group 3 required a much higher add compared to groups 1 and 2, the difference being statistically significant (p < 0.001). This

was in spite of all patients reading N6 on the Snellens near vision type. This difference could be due to different accommodative amplitudes and reserves in different persons, which decreases as the person grows older. This decrease was not apparent while testing using the standard near vision charts, but became evident as an increasing amount of plus add required to view the near target at baseline, indicating that probably subtle changes are poked up by the machine earlier than other methods.

The only complication we noted was mild stinging immediately following the application of the drops which lasted for less than 2 minutes. Mild lid retraction occurred in 10 eyes which received the combination drop. Phenylephrine is known to cause systemic toxicity like elevated blood pressure, arrhythmias and myocardial infarction. However, we did not check blood pressure or any other systemic parameters before and after drop instillation and hence cannot comment upon the occurrence of any systemic complications induced by the combination drug. This study did not establish the efficacy of tropicamide or the combination drop as a mydriatic or cycloplegic in the presence of systemic and local pathology. The cycloplegia and residual accommodation caused by the two drops were comparable, with no statistically significant difference between the two drops. We noted a mean hyperopic shift (latent error) occurring in the refractive error in both groups, due to the induced cycloplegia. The cycloplegia and residual accommodation were adequate in all the three age groups studied, indicating that the combination drop is effective even in younger patients who are known to have a higher accommodative tone. In this study we also suggest a method to directly measure the amount of cycloplegia caused by a drug, using the autorefractometer, calculated as the difference in the near add before and after instillation of drops. Earlier reports suggest the use of residual accommodation as an indicator of the amount of cycloplegia; this method of directly calculating the amount of induced cycloplegia has not been reported earlier, to the best of our knowledge.

CONCLUSION

In the eyes that received Tropicamide 1%, the mean cycloplegia measured at 20 minutes was 1.12 D and the mean residual accommodation was 1.20 D. In the eyes that received the combination drop, the mean cycloplegia was 1.05 D and the mean residual accommodation was 1.26 D. Though the cycloplegic effect of tropicamide 1% was marginally better than the combination drop, the difference in the two groups was not statistically significant for cycloplegia (p=0.007) or residual accommodation (p=0.15). A single drop of a combination of 0.8% tropicamide and 5% phenylephrine achieves adequate cycloplegia, in patient 11- 40 years of age.

REFERENCES

1. P.L. Kaufman, Accommodation and presbyopia: neuromuscular and biophysical aspects, in Adler's Physiology of the Eye: Clinical Application, Mosby, St. Louis,Mo, USA, 1992.

2. H. M. Culhane, B. Winn, and B. Gilmartin, Human dynamicclosed-loop accommodation augmented by sympathetic inhibition, Investigative Ophthalmology and Visual Science,1999;40(6):1137–43.

3. D. H. McDougal and P. D. Gamlin, Autonomic control of the eye, Comprehensive Physiology,2015;5(1):439–473.

4. N. L´opez-Gil et al. Retinal image quality during accommodation, Ophthalmic and Physiological Optics, 2013;33(4):497–507.

5. L. A. Ostrin and A. Glasser, The effects of phenylephrineon pupil diameter and accommodation in rhesus monkeys, Investigative Ophthalmology and Visual Science, 2004;45(1):215–221.

6. R. D. Biggs, M. Alpern, and D. R. Bennett, The effect of sympathomimetic drugs upon the amplitude of accommodation, American Journal of Ophthalmology, 1959; 48(1):169–172.

7. H. W. Leibowitz and D. A. Owens, Night myopia and the intermediate dark focus of accommodation, Journal of the Optical Society of America,1975;65(10):1121–1128.

8. L. F. Garner, B. Brown, R. Baker, and M. Colgan, The effect of phenylephrine hydrochloride on the resting point of accommodation, Investigative Ophthalmology and Visual Science,1983;24(4):393–395.

9. C. Zetterstrom, The effect of phenylephrine on the accommodative process in man, Acta Ophthalmologica, 1984;62(6):872–878.

10. J. Mordi et al. Effects of 0.1% cyclopentolate or 10% phenylephrine on pupil diameter and accommodation, Ophthalmic and Physiological Optics, 1986; 6(2): 221–227.

11. J. A. Mordi, W. M. Lyle, and G. Y. Mousa, Effect of phenylephrine on accommodation, American Journal of Optometry and Physiological Optics,1983;63(4):294–297.

12. C. Zetterstrom and R. Hahnenberger, Pharmacological characterization of human ciliary muscle adrenoceptors in vitro, Experimental Eye Research,1988;46(3):421–430.

13. G. Gimpel, M. J. Doughty, and W.M. Lyle, Large sample study of the effects of phenylephrine 2.5% eye drops on the amplitude of accommodation in man, Ophthalmic and Physiological Optics, 1994;14(2):123–128.

14. M. L. Eyeson-Annan, L. W. Hirst, D. Battistutta, and A. Green, Comparative pupil dilation using phenylephrine alone or in combination with tropicamide, Ophthalmology,1998;105(4):726–732.

15. T. Do, S. Kasthurirangan, L. Ostrin, and A. Glasser, The effects of phenylephrine on accommodation in humans, Optometry and Vision Science,2002;79:174.

16. S. Sarkar, A. M. Hasnat, and S. R. Bharadwaj, Revisiting the impact of phenylephrine hydrochloride on static and dynamic accommodation, Indian Journal of Ophthalmology,2012;60(6):503–09.

17. K. Richdale, M. D. Bailey et al. The effect of phenylephrine on the ciliary muscle and accommodation, Optometry & Vision Science, 2012;89(10):1507–11.

18. P. Bernal-Molina, A. J. Del ´Aguila-Carrasco, N. Lopez-Gil et al., Effect of phenylephrine on static and dynamic accommodation, in Proceedings of the ARVO Annual Meeting Abstracts, Seattle, Wash, USA, 2016.

19. J. C. Chen, K. L. Schmid, and B. Brown, The autonomic control of accommodation and implications for human myopia development: a review, Ophthalmic and Physiological Optics, 2003;23(5): 401–422.

20. B. Gilmartin, A review of the role of sympathetic innervation of the ciliary muscle in ocular accommodation, Ophthalmic and Physiological Optics,1986;6(1):23–37.

Source of Support: Nil. **Conflict of Interest:** None Declared.

Cite this article as: Sedhu P.A, Archana Pushpakaran, Cyriac Kurian. Effect on Ciliary Muscles and Accommodation: Comparative Study between Topical Tropicamide 1% versus Combination of Tropicamide 0.8% and Phenylephrine 5%. Int J Med Res Prof. 2017 Sept; 3(5):323-27. DOI:10.21276/ijmrp.2017.3.5.064