REVIEW

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Comparison of cycloplegic and mydriatic effect between cyclopentolate, tropicamide, and combination in children: a narrative review

Fany Gunawan[1*], Irawati Irfani[1,2], Feti Karfiati Memed[1,2], Mayasari Wahyu[1,2], Primawita Oktarima Amiruddin[1,2], Sesy Caesarya[1,2]

[1]Ophthalmology Department, Faculty of Medicine Padjadjaran University, Bandung, Indonesia;
[2]Pediatric Ophthalmology Division of Cicendo National Eye Hospital, Bandung, Indonesia.

*Corresponding to:
Fany Gunawan;
Ophthalmology Department, Faculty of Medicine Padjadjaran University, Bandung, Indonesia;
ceciliafany@gmail.com

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ABSTRACT

Introduction: Cycloplegic refraction is essential in pediatric eye examination. Inadequate cycloplegia provides inaccurate refraction so that therapeutic approaches become inappropriate. The ideal cycloplegic agent should have a rapid onset of action, quick recovery, adequate cycloplegia, without local or systemic side effects. None of the currently available drugs fulfil all of these criteria. To compare the cycloplegic and mydriatic effect of cyclopentolate, tropicamide, and their combination in children.

Methods: A comprehensive literature search was performed in PubMed, ScienceDirect, and Cochrane Library by entering keywords: "cyclopentolate", "tropicamide", "cycloplegia", "cycloplegic", "mydriasis", and "pupillary dilation". The search was limited to articles in English and published between January 2000 and November 2019. The findings from the related articles were presented as narrative reviews.

Result: Twelve articles were eligible to the review process. Four articles were conduct in subjects with dark irides. The cycloplegic agents used were tropicamide, cyclopentolate, and their combination, with or without phenylephrine.

Conclusion: Cyclopentolate, tropicamide, and their combination is widely used to achieve maximum cycloplegia. Several factors, such as age, iris color, and refractive status, need to be considered in the selection of dose, concentration, and regimen(s) of cycloplegic agents.

Keywords: cyclopentolate, tropicamide, cycloplegia, mydriasis, cycloplegic, pupillary dilation.
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INTRODUCTION

Cycloplegic refraction is essential in pediatric eye examination, especially in patient with high hyperopia, young children, and strabismus. Cycloplegic agents prevent the action of acetylcholine at muscarinic receptor sites, results in inhibition of accommodation because of paralysis of the ciliary muscles. Maximum cycloplegia in children is required for accurate measurement of refractive error because it maximally inhibits accommodation and prevents underestimation of hyperopia and overestimation of myopia.[1-4]

Instillation of a cycloplegic agent also results in mydriasis (pupillary dilation) due to paralysis of the pupillae sphincter muscle. Adequate pupillary dilation is important for evaluation of posterior segment in diagnosis of amblyopia and facilitates evaluation in retinoscopy. Certain cycloplegics have produced mydriasis but very little accommodative suppression. The different time courses of mydriasis and cycloplegia cause the pupil size as a poor indicator of the cycloplegic effect. Most ophthalmologists wait until the pupils are maximally dilated or the light reflexes are absent to perform cycloplegic refraction. This can result in unnecessary long waiting time or inaccurate measurement if maximum cycloplegia develop before or after maximum pupillary dilation or absence of pupillary reaction.[1-3]

The ideal cycloplegic agent should have a rapid onset of action, quick recovery, adequate cycloplegia, without local or systemic side effects. None of the currently available drugs fulfil all of these criteria. Atropine is the gold standard for maximum cycloplegia, but its slow onset, prolonged blur vision, long recovery time, and severe adverse effects have limited the application of this agent. Two of the most commonly used agents are cyclopentolate and tropicamide. Cyclopentolate is a drug of first choice for all ages in excellent short-term cycloplegia. Its cycloplegic effects begin at 25 – 75 minutes after instillation and recovery appears through 6 – 24 hours later. Disadvantages of cyclopentolate are poor cornea penetration and significant binding to iris melanin, in order that multiple doses or higher concentration are required for subjects with dark irides. Tropicamide has a faster onset with cycloplegia effect appears 20 – 30 minutes after administration, and recovery appears

6 hours later. It has a rapid penetration and a lack of binding to iris melanin. However, the cyclopegic effect is not strong enough as cyclopentolate and inadequate for children with hyperopia when used alone.[4-12]

Many clinicians have turned to combine cyclopentolate and tropicamide; often added with phenylephrine for maximize the mydriatic effect. There are no guidelines for an optimal regimen in children. Several studies have been conducted to compare the cycloplegic and mydriatic effect of these agents or their combinations, but different results have been reported.[1,4,6,8,10-12] Due to its inconsistencies, this literature review aims to compare the cycloplegic and mydriatic effect of cyclopentolate, tropicamide, and their combination in children.

MATERIALS AND METHODS

The search was conducted through electronic databases providing journal articles, such as PubMed, ScienceDirect, and Cochrane Library database by entering combination of keywords: "cyclopentolate", "tropicamide", "cycloplegia", "cycloplegic", "mydriasis", and "pupillary dilation". The search performed in December 2019 until January 2020. Abstracts were reviewed to choose articles that were related to the study purpose based on the keywords. The complete studies related to the abstract were then screened to meet the inclusion and exclusion criteria. The inclusion criteria were all studies that with human subjects, reporting children who underwent cyclopegic refraction or pupillary dilation using cyclopentolate, tropicamide, or combination of these regimens. Studies were excluded if the full text could not be accessed. The search was limited to articles in English and published between January 2000 and November 2019. The findings from the search were presented as narrative reviews.

RESULTS

The literature search identified 127 articles that were related to the keywords. As many as 59 duplicated titles were removed. Abstracts were screened and 22 articles related to the study purpose. Finally, only 12 articles were eligible to the review process. The articles flow is presented in Figure 1.

Information was taken from each included article on: (1) characteristics of participants, consisting of age, iris color, and inclusion criteria, (2) type of intervention including regimen(s) used, concentration, number of administrations, timing of dosing; (3) type of outcome measured and its results. The articles were summarized in a matrix format (Table 1).

DISCUSSION

Inadequate cycloplegia in children provides inaccurate refraction so that therapeutic approaches become inappropriate; however, an overdose of cycloplegics can cause drug reactions or discomfort to the patient. The unpleasant nature of administering eyedrops especially in children may hinder completion of the examination. There are no guidelines for optimal regimen for sufficient cycloplegia in children.[4,13]

Tropicamide and cyclopentolate are cycloplegic drugs commonly used for routine ophthalmologic examination in children that have different strengths and depths in cycloplegic and mydriatic actions. Cyclopentolate has stronger cycloplegic effect than tropicamide, but has been associated with central nervous system side effects. Tropicamide is the fastest acting but it is relatively weak. Ihekaire et al. demonstrated that 1% cyclopentolate provided a greater reduction in the amplitude of accommodation and mean additional pupil size than did 0.5% tropicamide at 17-29 years of age. In children, Pi et al. showed cycloplegic effect of 1% cyclopentolate is more complete than 0.5% tropicamide at 6 – 15 years of age resulting in a significantly higher average diopter using cyclopentolate than tropicamide.[8,18,19]

Tropicamide does not bind to iris melanin. Chng et al. states that in people with dark irides, 1% tropicamide has the same cycloplegic effect, but higher mydriatic effect, than 1% cyclopentolate. Two drops of tropicamide are recommended for maximum cycloplegic effect in subjects with dark irides in cases where atropine is not required.

The cycloplegia effect is influenced by several factors such as age, iris color, and refractive status. Cyclopentolate has a stronger effect that more obvious in younger children and hyperopia. However, its cycloplegic effect was reduced in subjects with dark irides due to the significant binding to iris melanin resulting in reduced substance to ciliary receptors. Tropicamide has a weaker binding to iris melanin. Chng et al. stated that in people with dark irides, 1% tropicamide has a similar cycloplegic effect, but higher the mydriatic effect, rather than 1% cyclopentolate. Two drops of tropicamide were recommended for maximum cycloplegic effect in subjects with dark irides in cases where atropine is not required.[8,9,12]

Many clinicians have turned to find effective cycloplegic regimens in children, such as increasing the dose of cyclopentolate or tropicamide. Bagheri et al. demonstrated a single drop of 1% cyclopentolate was adequate for cycloplegic refraction with fewer side effects when compared to multiple doses. Siderov et al. also showed similar results regarding mydriatic effect of tropicamide. A single drop of 0.5% tropicamide provides satisfactory pupillary dilation of at least 6 mm. Administering of two drops of 0.5% tropicamide produced a

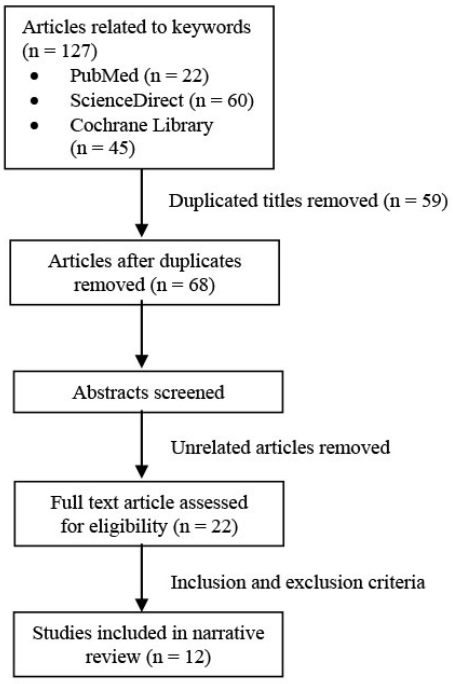

Figure 1. Flowchart of the study selection process

greater statistically significant in pupillary diameter compared with single drop, but the difference was not clinically significant.[13,20]

The combination of tropicamide and cyclopentolate is also widely used to achieve maximum cycloplegia. Phenylephrine is often added to maximize mydriatic effect. Ebri et al. showed that combination of 0.5% tropicamide and 1% cyclopentolate was more effective than multiple doses of 1% cyclopentolate. Minderhout et al. also demonstrated similar results, particularly in medium pigmented subjects. Tropicamide combined with cyclopentolate synergistically enhances the cycloplegia effect in children, while remaining the faster onset. These results differ from study by Sherman et al. The study showed combination of 1% tropicamide and 1% cyclopentolate, added with 2.5% phenylephrine, elicited equivalent cycloplegic and mydriatics effects compared with 1% cyclopentolate combined with 2.5% phenylephrine, but produced slightly larger pupils that were less responsive to light in patients with dark irides. In addition, especially in children under 5 years of age with high hyperopia (SE≥5 D) or fully accommodative esotropia, Yoo et al. showed the combination of 0.5% tropicamide, 1% cyclopentolate, and 0.5% phenylephrine gave a weaker cycloplegic effect than 3 – 4 drops of 1% cyclopentolate, but the difference was small. There was no significant difference in patients older than 5 years.[1,5,6,12,14,21]

The cycloplegic effect in combination of tropicamide and cyclopentolate was compared with atropine. Sani et al. showed 1% tropicamide combined with 1% cyclopentolate produced a similar cycloplegic effect with 1% atropine. This result was different from Fan et al., Ebri et al., and Minderhout et al. which stated 1% atropine is still the most effective cycloplegic agent.[5,7,12,14,21]

Table 1. Characteristics and summary of included articles

No	Author	Location	Subject (person)	Inclusion criteria	Regimens	Treatment	Outcome	Results
1	Fan et al. (2004)	Hong Kong	25	Age : 2- 10 years Hyperopia >2.50D in at least one eye Dark irides	• I : 0.5%T + 0.5%P (TP) • II : 1%C + 1%T (TC) • III : 1%A eo	• I and II: One drop of each agent three times at interval of 15 min • III : twice daily for 3 days	Cycloplegia, mydriasis	• 1%A was the most effective cycloplegic agent, followed by TC then TP. • TC was statistically significant provides greater mean total refraction rather than TP in younger children (≤5 years of age) and strabismus, but similar in children >5 years of age. • No significant difference in mean pupillary diameter among those regimens.
2	Chng et al. (2005)	Singapore	174	Age : 3 – 12 years Dark irides	• 1%T multiple doses with or without minute intervals • I%C multiple doses with or without minute intervals	• I : 1 drop of 1%C and 1%T with 10 second interval (CC) • II : 1 drop of 1%T and 1%T with 10 second interval (TT) • III : 1 drop of 1%C and 1%T with 5 minute interval (C/5min/T). • IV : 1 drop of 1%T and 1%T with 5 minute interval (T/5min/T).	Cycloplegia	• All groups had similar differences in autorefraction after cycloplegia. TT had a slightly larger difference but not statistically significant. • T has a superior mydriatic effect and similar cycloplegic effect rather than C in people with dark irides. • Two drops of tropicamide can replace cyclopentolate combination for maximum cycloplegic effect in Chinese children and others with dark irides in cases where atropine is not required.
3	Bagheri et al. (2007)	Tehran, Iran	96	Age : 3.5 – 20 years	• 1%C (single, multiple doses)	• I : one drop compared with 2 drops • II : 2 drops compared with 3 drops • III : 1 drop compared with 3 drops • Interval : 5 minutes	Cycloplegia	• A single drop of C1% provides adequate cycloplegia effect in children and young patients with any type of strabismus or refractive error. • Higher doses of cyclopentolate do not result in better cycloplegia but cause more complications.

No	Author	Location	Subject (person)	Inclusion criteria	Regimens	Treatment	Outcome	Results
4	Ebri et al. (2007)	South Eastern Nigeria	233	Age : 4 – 15 years	• I : 1%A • II : 1%C multiple doses (CC) • III : 1%C + 0.5%T (TC)	• I : 1 drop three times daily for 3 days • II : 2 single drops with interval 5 minutes • III : 1 drop of each with interval 5 minutes	Cycloplegia, mydriasis	• 1%A was a more effective cycloplegic agent than TC or CC. • TC provided a smaller percentage of subject with >0.5D of residual accommodation, and greater percentage of subject with adequate pupil dilation and negative pupillary reflex, rather than CC.
5	Park et al. (2009)	Daegu, Korea	50	Age : 3 – 41 years	• 1%T (single, multiple doses) • 2.5%P (single, multiple doses) • 2.5% P + 1%T (TP)	• I : 1 drop 1%T in RE; 1 drop of 2.5%P in LE. • II : 2 single drops of 1%T in RE; one drop each of 2.5%P and 1%T in LE • III : 2 single drops of 2.5%P in RE; 1 drop each of 2.5%P and 1%T tropicamide in LE • Interval : 5 minutes	Mydriasis	• 1%T was more effective at inducing pupillary dilation than 2.5%P. • TP was more effective than multiple drops of single eye drops.
6	Anderson et al. (2010)	Texas, USA	45	Age : 4–32 years Dark irides (brown or dark brown)	• I : 1%T + 2.5% P (TP) • II : 1%T + 1% C (TC)	• One drop of each agent	Mydriasis	• In dark irides, TP had similar results in percentage of subjects reaching a 6 mm pupil diameter. • TP had a greater number of subjects reaching the 7 mm pupil than TC with a shorter time to reach that size.
7	Pi et al. (2011)	China	1907	Age : 6 – 15 years	• I: 0.5%T multiple doses (TT) • II: 1%C multiple doses (CC)	• 3 drops of each drug with 10 minutes interval	Cycloplegia	• The cycloplegic effect of C was stronger than T.
8	Sani et al. (2016)	Kano, Nigeria	63	Age : 5-12 years Hyperopia ≥1 D in each eye	I : 1%A II: 1%C + 1%T (multiple doses) (TC)	I : one drop twice daily for 3 days II : 2 single drop of each drugs with 5 minutes interval	Cycloplegia	• TC showed no significant difference in mean spherical equivalent compared with 1%A. • TC had cycloplegic effect comparable to 1%A with less severe side effects and shorter duration of action.
9	Sedhu et al. (2017)	Kerala, India	150	Age : 11 – 40 years	I : 1%T II : 0.8%T + 5%P (fixed combination) (TP)	One drop of each agent	Cycloplegia	• Cycloplegic effect was better in T than TP, but not statistically significant.

No	Author	Location	Subject (person)	Inclusion criteria	Regimens	Treatment	Outcome	Results
10	Yoo et al. (2017)	Seoul, Korea	308	Age : <14 years Hyperopia with SE >+1.00D at least one eye measured by cycloplegic refraction	I: 1%C + (0.5%T + 0.5P; fixed combination) (TCP) II : 1%C multiple dose (CC)	I : one drop of 1%C followed by 2-3 drops of combination with 15 minutes interval II : 3-4 drops with 15 minutes interval	Cycloplegia	• CC had a stronger cycloplegic effect than TCP, especially in children under 5 years of age with high hyperopia (SE≥5 D) or fully accommodative esotropia. • There was no significant difference in patients >5 years, regardless of the presence of high hyperopia or fully accommodative esotropia.
11	Sherman et al. (2019)	Chicago, Illinois, USA	75	Age : 4 – 11 years	I : 1%T + 1%C + 2.5%P (TCP) II : 1%C + 2.5%P (CP)	One drop of each agent	Cycloplegia, mydriasis	• TCP and CP showed equivalent cycloplegic effects with similar results in mean differences of spherical equivalent. • All pupils dilated to ≥6.0 mm. TCP had a greater proportion of ≥7.0 mm pupil dilation, but not significantly different. • A significant interaction between regimen and iris pigmentation was found in pupil dilation and percentage constriction, whereas no significant on cycloplegic effects. • TCP showed slightly larger pupils that were less responsive to light only in subjects with dark irides.
12	Minderhout et al. (2019)	Hague, Netherlands	67	Age : 3 – 6 years	I : 1%C multiple doses (CC) II : 1%C + 1%T (TC) III : 0.5%A	I : 2 single drops of 1%C with 5 minute interval II : 1 drop of 1%C then 1%T with 5 minute interval III : twice daily for 2 days before appointment and once in the morning of the day of appointment	Cycloplegia	• 0.5%A provided the highest hypermetropic values compared to CC and TC. • TC provided clinically better results than CC and equal to A in medium pigmented subjects.

T : tropicamide; C : cyclopentolate; P : phenylephrine; A : atropine; TT : tropicamide with multiple doses; CC : cyclopentolate with multiple doses; TC : tropicamide-cyclopentolate; TP : tropicamide-phenylephrine; TCP : tropicamide-cyclopentolate-phenylephrine; eo : eye ointment; RE : right eye; LE : left eye

The combination of tropicamide and cyclopentolate also has adequate mydriatic effect. Adequate pupillary dilation is important for evaluation of posterior segment in diagnosis of amblyopia and facilitates evaluation in retinoscopy. Ebri et al. showed the combination of 0.5% tropicamide and 1% cyclopentolate result in greater percentage of subject with adequate pupillary dilation and negative light reflect when compared with 2 drops of 1% cyclopentolate. Anderson et al. showed 1% tropicamide combined with 1% cyclopentolate had the same results in 6-mm pupillary dilation compared combined with 2.5% phenylephrine in eyes with dark irides. Fan et al. showed there was no significant difference on pupillary diameter between 1% atropine, 1% tropicamide-1% cyclopentolate, and 0.5% tropicamide-0.5% phenylephrine in subjects with dark irides.[5,14,16]

The limitation of the study is the literature search based on keywords that are determined, so some contributions may not be summarized. Further clinical research is needed to evaluate the effectiveness of cyclopentolate, tropicamide, and their combination on cycloplegics and mydriasis in children, especially with dark irides.

CONCLUSION

None of the currently available drugs fulfill the criteria of ideal cycloplegic agents. Cyclopentolate has stronger

cycloplegic effect, but it reduced in subjects with dark irides and associated with central nervous system side effects. Tropicamide is the fastest acting and less binding to iris melanin, but its cycloplegic effect is relatively weak. Cyclopentolate, tropicamide, and their combination is widely used to achieve maximum cycloplegia. Several factors, such as age, iris color, and refractive status, need to be considered in the selection of dose, concentration, and regimen(s) of cycloplegic agents.

CONFLICT OF INTEREST

The authors confirm that this article content has no conflicts of interest.

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Authors don't have any financial disclosure.

AUTHOR CONTRIBUTION

The authors are equally contributed to the study since the conceptual framework until reporting the results.

REFERENCES

1. Sherman AE, Shaw MM, Ralay-Ranaivo H, Rahmani B. Tropicamide has limited clinical effect on cycloplegia and mydriasis when combined with cyclopentolate and phenylephrine. *J AAPOS*. 2019:2.e1-30.e5. doi:10.1016/j.jaapos.2018.08.012
2. Kyei S, Nketsiah AA, Asiedu K, Awuah A, Owusu-Ansah A. Onset and duration of cycloplegic action of 1% cyclopentolate – 1% tropicamide combination. *Afr Health Sci*. 2017;17(3):923-932. doi:10.4314/ahs.v17i3.36
3. Laojaroenwanit S, Layanun V, Praneeprachachon P, Pukrushpan P. Time of maximum cycloplegia after instillation of cyclopentolate 1% in children with brown irises. *Clin Ophthalmol*. 2016;10:897-902. doi:10.2147/OPTH.S102611
4. Yazdani N, Sadeghi R, Momeni-Moghaddam H, Zarifmahmoudi L, Ehsaei A. Comparison of cyclopentolate versus tropicamide cycloplegia: A systematic review and meta-analysis. *J Optom*. 2018;11:135-143. doi:10.1016/j.optom.2017.09.001
5. Fan DSP, Rao SK, Ng JSK, Yu CBO, Lam DSC. Comparative study on the safety and efficacy of different cycloplegic agents in children with darkly pigmented irides. *Clin Exp Ophthalmol*. 2004;32:462-467. doi:10.1111/j.1442-9071.2004.00863.x
6. Yoo SG, Cho MJ, Kim US, Baek S-H. Cycloplegic refraction in hyperopic children: Effectiveness of a 0.5% tropicamide and 0.5% phenylephrine addition to 1% cyclopentolate regimen. *Korean J Ophthalmol*. 2017;31(3):249. doi:10.3341/kjo.2016.0007
7. Sani RY, Hassan S, Habib SG, Ifeanyichukwu EP. Cycloplegic effect of atropine compared with cyclopentolate-tropicamide combination in children with hypermetropia. *Niger Med J* 2016;57: 173-177. doi:10.4103/0300-1652.184065
8. Pi LH, Zhao JL, Liu Q, et al. Comparison of cycloplegic retinoscopy using cyclopentolate or tropicamide eye drops in an epidemiologic study of pediatric refraction among 1907 school-aged children. *Sci Res Essays*. 2011;6(3):635-640. doi:10.5897/SRE10.1018
9. Chng O, Jones N, Kian KB, Ming KH, Kee S. Is tropicamide a more effective cycloplegic than cyclopentolate in children with dark irides? *Australian Orthoptic Journal,* 2005; 38:2-4.
10. Egashira SM, Kish LL, Twelker JD, Mutti DO, Zadnik K, Adams AJ. Comparison of cyclopentolate versus tropicamide cycloplegia in children. *Optom Vis Sci.* 1993; 70:1019-1026. doi:10.1097/00006324-199312000-00005
11. Gupra SK. Mydriatics and Cycloplegics. In: Gupra SK, Agarwal R, Srivastava S, eds. *Textbook on Clinical Ocular Pharmacology and Therapeutics*. New Delhi, India: Jaypee Brothers Medical Publishers; 2014:87-95. doi:10.5005/jp/books/12384
12. Minderhout HM, Joosse M V, Grootendorst DC, Schalij-Delfos NE. A randomized clinical trial using atropine, cyclopentolate, and tropicamide to compare refractive outcome in hypermetropic children with a dark iris; skin pigmentation and crying as significant factors for hypermetropic outcome. *Strabismus*. 2019;27(3):127-138. doi:10.1080/09273972.2019.1629466
13. Bagheri A, Givrad S, Yazdani S, Mohebbi MR. Optimal dosage of cyclopentolate 1% for complete cycloplegia: A randomized clinical trial. *Eur J Ophthalmol*. 2007;17(3):294-300. doi:10.1177/112067210701700303
14. Ebri A, Kuper H, Wedner S. Cost-effectiveness of cycloplegic agents: Results of a randomized controlled trial in Nigerian children**.** *Invest Ophthalmol Vis Sci*. 2007; 48:1025-1031. doi: 10.1167/iovs.06-0604
15. Park JH, Lee YC, Lee SY. The comparison of mydriatic effect between two drugs of different mechanism. *Korean J Ophthalmol*. 2009;23(1):40-42. doi:10.3341/kjo.2009.23.1.40
16. Anderson HA, Bertrand KC, Manny RE, Hu YS, Fern KD. A Comparison of two drug combinations for dilating dark irides. *Optom Vis Sci*. 2010;87(2):120-124. doi:10.1097/OPX.0b013e3181cc8da3
17. Sedhu PA, Pushpakaran A, Kurian C. 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; 3(5):323-327. doi:10.21276/ijmrp
18. Ihekaire DE. The comparative efficacy of cyclopegic drugs–tropicamide and cyclopentolate on school children. *International Journal of Scientific Research in Education*. 2012; 5(3):223-246.
19. Patel AJ, Simon JW, Hodgetts DJ. Cycloplegic and mydriatic agents for routine ophthalmologic examination: A survey of pediatric ophthalmologists. *J AAPOS*. 2004;8:274-277. doi:10.1016/j.jaapos.2004.01.004
20. Siderov J, Nurse S. The mydriatic effect of multiple doses of tropicamide. *Optom Vis Sci* 2005; 82:955–958. doi:10.1097/01.opx.0000187847.48093.55
21. Kleinstein RN, Mutti DO, Manny RE *et al.* Cycloplegia in African-American children. *Optom Vis Sci* 1999; 76:102-107.