CYCLOPENTOLATE VERSUS TROPICAMIDE AND CYCLOPENTOLATE IN LIBYAN CHILDREN

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ABSTRACT

The young children have very strong ciliary muscle tone, that need cycloplegic agents to paralyze it, which done by instilling of cycloplegic eye drop. As eye drop usage in young is challenge. The frequent use cycloplegic drugs and the duration needed for cycloplegia to tack place, both bring the child to get bored. The aim of this study is to make cycloplegic refraction procedure shorter with less apply of eye drop. The study conducted as cross-sectional study on 40 Libyan children, between 3- 4 years old with dark iris, where two regimens (cyclopentolate 1% as a regimen 1 and cyclopentolate 1% with tropicamide 1% as regimen 2) was applied on each eye of same person at same time (to minimize bases due to change in machine or surrounding factors). The refraction is measured after application of those regiment three time, with 10 minutes interval. The refraction was measured by autorefractometer ± retinoscope when needed, the changes in spherical equivalent was used to determine maximum cycloplegia of each regimen at certain point of time. The result showed that there is mild difference between 30 and 40 minutes in regimen 1 (42.5%: 40% subsequently), in compare to regimen 2, maximum cycloplegia occurred at 30 minutes (50% of cases). The frequency of maximum dilatation at 50 minutes was 17.5% in regimen 1 and 12.5 % in regimen 2. This indicate that maximum cycloplegia occurred at 30 minutes in regimen 2. We concluded the effectiveness of regimen 2 in fasting onset of maximum cycloplegia only after twice eye drop, which saving time and effort without effect on cycloplegic outcome.

KEY WORDS: Tropicamide, Cyclopentolate, Cycloplegic refraction in children

INTRODUCTION

The refraction of the eye:

Normally, when the lights reflect from any object to the eye, its rays undergo a refraction mechanism to focus on the retina to create a clear retinal image, this done by the cornea (main refractive structure of the eye) and the lens. When this process is done in a perfect way, the state of the eye called emmetropia (figure 1). However, when the reflected rays from an object don't focus on the retina, they will create a blurred retinal image, the state called ametropia (1).

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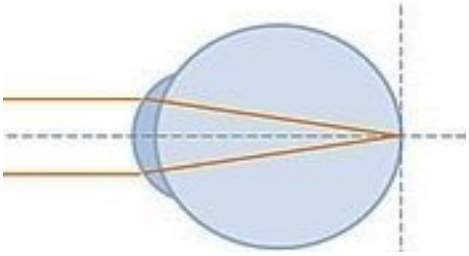

Figure 1: Illustrates the position of reflected rays on the retina in emmetropia.

Classification of the refractive error:

As emmetropia occur when the image of the object falls on the retina, the ametropia occur when the image focus in front or behind the retina, which divided into:

1-Nearsightedness or myopia: occur when the image of the object created in front of the retina, result in blurred image for far, with relatively clear image for the near (figure 2). Myopia usually more common in the adult, less common in the children (1% of rural Nepalese, 4% of south Africans, 12% of US population), myopia corrected either by concave glasses, contact lens or refractive surgery (2).

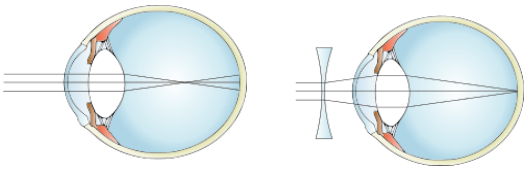

Figure 2: Shows the position of image that creating in myopic eye (first image) & how its position change by corrected glasses (second image) to make clear image.

2-Far-sightedness or hyperopia or hypermetropia: where the image falls behind the retina, person with this type of refractive error usually able to see relatively clear far object with blurred near object, which need more accommodation to overcome this near blurred vision (Figure 3) (3). It could be mild hyperopia (< +2.00Ds), moderate (between +2.25 to +5.00Ds) and high hyperopia (> 5.25Ds) (4). It affected primary the young children with 8% at six years and 1% at fifteen years. This type of error can be correct by either convex lenses, contact lens or refractive surgery (3).

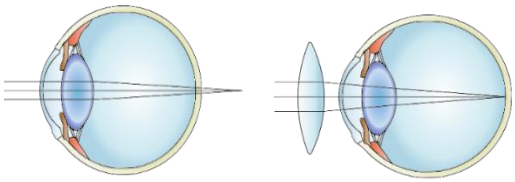

Figure 3: Shows the position of image in hyperopia and its correction by convex lens.

3-Astigmatism: secondary to imperfect spherical shape of either cornea (corneal astigmatism), lens (lenticular astigmatism) or both, where the image is always burred at all distances (figure 4). It can be corrected by cylinder and Toric lenses as well as contact lens.

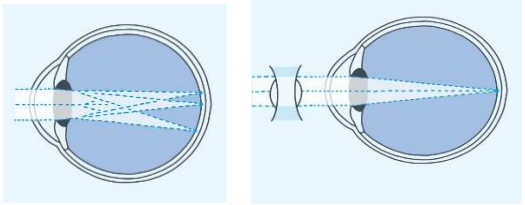

Figure 4: Astigmatism (upper image, where image can't focus on one point, and its correction by cylinder lens.

The accommodation and its function:

Accommodation is the ability of the eye to change its power to focus the image of seeing near objects. This occurs due to increase the power of the crystalline lens of the eye. Relaxation of the zonules allows the lens to becomes more spherical by change its capsule shape, increase its curvature and its anteroposterior diameter leading to the increase of its dioptric power (passive accommodation). The active component of accommodation is caused contraction of circular part of the ciliary muscle leading too relaxation of the zonulas, (figure 5). Cycloplegic drugs are used to abolish the ciliary muscle function reaching a state of cycloplegia.

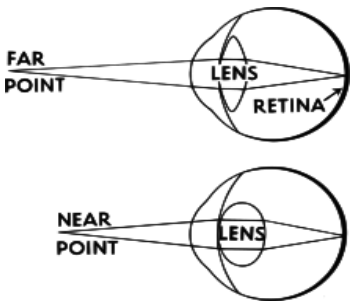

Figure 5: Illustrates the change in the shape of the crystalline lens for far (upper image) to near (lower image).

The distance between the near point and far point is called the accommodation range, which is very large in children, and decrease with age. The near reflex, is induced when the eye changes its focus from far to near, it is composed of three processes (accommodation of the lens by increase its convexity, constriction of the pupil to increase the depth of focus, and converging of the eyes to have similar parity of both eyes (5).

Cycloplegic refraction and its benefit:

Cycloplegic refraction is the procedure to measure the total refractive error by temporary paralysis of ciliary muscle, eliminating any effort of accommodation. This is achieved by cycloplegic eye medication, which could be in the form of drops or ointment.

In children the accommodation is very strong giving them ability to change their refractive power, so they are unable to control their focusing leading to false estimation of their refractive error, over myopia (6).

The measurement of cycloplegic refraction is done by retinoscope or autorefractometer.

The cycloplegic agents:

Cycloplegic agent is a drug which temporarily paralyze the ciliary muscle (loss of accommodation of lens). A mydriatic drug paralyze the sphincter muscle of the iris (induce mydriasis). Both groups are parasympatholytic having both functions to a variant degree and also in onset of action and duration of cycloplegia (Table 1). Parasympatholytic agents includes atropine, homatropine, scopolamine, cyclopentolate and tropicamide (7). Regarding to atropine which is one of most powerful cycloplegic and mydriatic agent, which present as 0.5% and 1% solution and ointment, with disadvantage of prolonged onset of action (six to twenty-four hours) and very long duration of action (ten to fifteen days) which interrupt daily activities of patient. The maximum cycloplegic effect occurs after 3 days of application. Side effects secondary to systemic absorption include, rapid pulse, fever, flushing, dry mouth and agitation with possibility of allergic reaction in the form of eczematous rash around the eye combined with conjunctival injection.

Table 1: Shows a comparison between some cycloplegic agents.

Drug	Onset	Duration
Atropine	6-24 hours	10-15 days
Homoatropine	1 hour	1-2 days
Scopolamine	30-60 minutes	3-4 days
Cyclopentolate	30-45 minutes	12-24 hours
Tropicamide	20-30 minutes	4-10 hours

On the other hand, cyclopentolate (cyclogyl, cylate, AK-pentolate) is a cycloplegic agent with less cycloplegic action but much more rapid onset (just thirty to forty-five minutes), shorter duration (six to twenty-four hours) and maximum cyclopregic effect at one hour. In compere to atropine those advantages make it a good option to replace atropine in some situation. Also, cyclopentolate has much less adverse effect in compere to atropine, where just occasionally the child could show sign of systemic toxicity secondary to systemic absorption. It is applied as a one drop, which can be repeated after five to ten minutes for two to three times. Its side effect includes burning sensation with irritation of the eye, temporary blurred vision, the serious side effect include irritation with dizziness and fainting, hallucination or even seizure, however, they are rare. It is available in form of 0.5%, 1% and 2%.

Moreover, tropicamide (mydiacyl, tropicacyl) which present as 0.5% and 1%, is another cycloplegic agent, weak but with more rapid onset (only twenty minute) with shorter duration (four to six hours) this advantage makes it the best choice

for fundus examination. Additionally, its weak cycloplegic effect can be used to relive ciliary spasm in anterior uveitis (so relive the pain) and induce mydriasis, so prevent posterior synechia or break it if it is present. In addition to the previous uses, tropicamide can be use in some objective refraction for those patients whose have weak accommodation, and they don't need strong cycloplegic refraction (7).

Measuring of maximum cycloplegia:

As the maximum cycloplegia is needed in young children to avoid underestimation of hypermetropia or overestimation of the myopia secondary to strong ciliary muscle. For cyclopentolate, the maximum cycloplegic effect starts between 10 to 60 minutes from fist drop application according to the age and color of the iris (8).

Literature review:

By looking to "Comparison of cyclopentolate versus tropicamide cycloplegia: A systematic review and meta-analysis" study, which aimed to compere cycloplegic efficacy of cyclopentolate and tropicamide. Where it presented meta-analysis of six study, the conclusion suggested that tropicamide could be another valid option to cyclopentolate with exception of some cases like infant, young children, high hyperopia and those whose examination result not match with manifested visual problem (9, 10). This conclusion can support our idea to use tropicamide with cyclopentolate to increase its onset and shorting the maximum cycloplegic effect (shorting examination process) and whole cycloplegic duration (rapid recovery of the patient).

Also, as mentioned by "Cycloplegic effect of atropine compared with cyclopentolate-tropicamide combination in children with hypermetropia" study, that compare cycloplegic effect of atropine 1% in one hand, with cyclopentolate 1% with tropicamide 1%, on sixty-three subject with hyperopia, aging between five to twelve years old, and spherical equivalent was the main parameter of comparison, the conclusion was that the combination of 1% cyclopentolate with 1% tropicamide could be an effected alternative regimen in compare to atropine for hyperopic children (11). This conclusion supports our study in efficacy of cyclopentolate with tropicamide combination.

Moreover, as illustrated by "Comparison of cyclopentolate versus tropicamide cycloplegia in children" that was double masked study, on twenty non-strabismic, non-amblyopic hyperopic children aging between six to twelve years old, where compare the cycloplegic effect of 1% tropicamide a to that for 1% cyclopentolate, they used both retinoscope, distance subjective refraction and autorefractometer. The result of refraction showing no statistic difference between two regimens in both retinoscope and distance subjective refraction, with difference in autorefractometer. Additionally, no refractive difference between thirty minutes and sixty minutes after instillation of the drop, also the accommodation inhibited more strongly by cyclopentolate in compare to tropicamide by autorefractometer, those lead to conclude that the tropicamide can be useful as a cycloplegic agent for school aged children with mild to moderate hyperopia (12), which also gives some support on our study.

Regarding to "onset and duration of cycloplegic action of 1% cyclopentolate - 1% tropicamide combination" study, that involved seventy-seven student aged between fifteen to twenty-five years old, aimed to study the time course of onset, time and duration of maximum cycloplegic effect and full duration of this effect, where it compare regimen of cyclopentolate 1% with tropicamide 1% as

combination and compare to with cyclopentolate 1% alone in same person (right eye for first regimen and left for cyclopentolate alone). The comparison parameter were subjective near add and pupil diameter, the measurement done after one hour from first instillation, with five minute interval, and continue up to seven hours, the result was that, the first regimen has rapid onset (five to ten minute) with shorter time to reach the maximum cycloplegic effect (fifty-five minutes for fist regimen and ninety minutes for second one) and rapid recovery (seven hours for first versus eight for second regimen) in majority of the cases (79.2%). And the conclusion was that clinically the combination of 1% cyclopentolate with 1% tropicamide is superior to 1% cyclopentolate alone in rapidity of the onset and reaching of maximum cycloplegic effect and rapid recovery (13). however, the age group is out from our age group study, but the goal of our study is the teat those regimens in younger age group to fill this gap.

As illustrated by "Cycloplegia in African-American children" study which concerned on the selection of the cycloplegic agent depends on the desired outcome, patient character and the associated risks, where refraction of patient measured after instillation of local anesthesia, followed by one drop of tropicamide 1% with one drop of cyclopentolate in both eyes, followed by frequent autorefractometer measurement at thirty, forty-five and sixty minutes, and the conclusion was that the combination of tropicamide 1% with cyclopentolate 1% is adequate cycloplegic and mydriatic with maximum cycloplegic effect at thirty minutes after first drop in African – American race (14). This study proves our study concern.

In compare to "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" study which compared between three regimens, first was atropine 0.5% (that applied twice daily for two and half days), second was two drops of cyclopentolate 1%, and last was one drop of 1% tropicamide followed with one drop of 1% cyclopentolate, those regimens applied on sixty-seven hyperopic children with dark iris, aging between three to six years old, in outpatient clinic as a double blind randomized study, where those children received two drop of 1% cyclopentolate in one eye and one drop of tropicamide 1% followed with one drop of 1% of cyclopentolate in other eye, then after two weeks, the refraction repeated with 0.5% atropine regimen, the main comparison parameter was spherical equivalent, also the comparison of spherical equivalent was done at first according to cycloplegic regimen (compare three regimens), then done according to sex, ethnicity and skin pigmentation (which divided to light, medium and dark). The result was that atropine regimen produced more hyperopia than other two regimens in same person. However, there was no significant difference between cyclopentolate regimen and combination of cyclopentolate with tropicamide. Moreover, skin color and ethnicity had strong relation in compare to gender that showed no association, additionally, the strongest association of cycloplegic effect with type of regimen that used, was for skin color. And the conclusion of this study was that, the 0.5% atropine has the highest hyperopic refraction, children with dark pigmented skin have lower hyperopic refraction by three regimen, in compare to medium skin pigmentation which showing equal hyperopic refraction between 0.5%

atropine regimen and combination of 1% tropicamide with 1% cyclopentolate., and lower hyperopia with 1% cyclopentolate regimen (15), this study increase the value of our study, where it mentioned that the cycloplegic effect of combination of cyclopentolate with tropicamide as the effect of atropine regimen, and stronger than cyclopentolate alone in medium skin pigmentation.

Supported by the "Eye color and skin pigmentation as significant factors for refractive outcome and residual accommodation in hypermetropic children: a randomized clinical trial using cyclopentolate 1% and tropicamide 1" study, which compare between two regimen (first two drop of cyclopentolate 1%), and second regimen (one drop of tropicamide 1%, followed by one drop of cyclopentolate 1%) in two hundred and fifty-one hyperopic children, whose classified according to skin and iris color (light, medium and dark color), as a double blind randomized study, and it concluded that the skin rather than iris pigmentation is the decisive parameter in determine the cycloplegic effect. Moreover, it mentions the need for awareness of cycloplegic limitation in dark pigmented iris, however the regimen of 1% tropicamide with 1% cyclopentolate has more accurate refraction both clinically and statically in dark skin with dark iris color (16). which also increase our study value.

METHODES

The study is a prospective cross section study, involved forty Libyan children, aged between three to fourteen years old. The study was conducted in Benghazi Eye Hospital outpatient clinic in Benghazi, Libya. All cases were referred to refraction room because of strabismus, poor vision or headache. All of the patients received one drop of 1% cyclopentolate in the right eye (regimen 1) and one drop of 1% tropicamide followed by one drop of 1% cyclopentolate immediately in left eye (regimen 2), after instillation of local eye drop anesthesia. The applications where repeated two times with ten-minute interval. The refraction was measured by autorefractometer and or retinoscope when autorefractometer was not possible at thirty (immediately after instillation of last drops), forty and fifty minutes from the first drop application. If the spherical equivalent changed by more than 0.5 D; another reading was taken at sixty minutes. If the reading was stable or there is a decrease between second and third reading; we suffice by previous readings.

The spherical equivalent for each reading was recorded. The refraction was measured in all of the cases in the first reading by autorefractometer, in the second and third reading retinoscopy was done in one non-cooperative child for auto refractometer. The change in the spherical equivalent was the main parameter to determine the point at which the refraction becomes stable or start to decrease and this point was consider as the maximum cycloplegic point. Then we compare the time at which cycloplegia reach its maximum between the two regimens. The hypermetropia were classified to mild (< 2.25 D), moderate (2.5 - 4.75 D) and sever (> 5.00D).

Also, the colour of the iris and skin were evaluated.

We exclude the children whose are known to be allergic to cyclopentolate or tropicamide, along with those with CNS problem or systemic disease that may affect the cycloplegic response, addition to those with intraocular disease or anomalous. Children younger than three years were excluded because usually they need general anesthesia for examination.

RESULTS

There were 24 females and 16 males, aged between three to fourteen years old (main age was 7±2) involved in this study, one of them with myopia, seven with mild hyperopia, three with high hyperopia, and remain with moderate hyperopia with thirteen of them have strabismus, two of them are known amblyopic with history of occlusion therapy. All of the cases found to have dark iris, two with black iris and remain with brown colour, with medium to dark skin (twenty with medium pigmented skin and remain with dark skin. Then we collect the spherical equivalent for regimens 1 (R1) and regimen 2 (R2) for each patient, then we calculate at which time was the maximum cycloplegic reading for each regimen in each eye for every patient separately. The result was that, for R1 the maximum cycloplegic effect (R1 max) was in seventeen participants (42.5%) at thirty minutes, in sixteen participants (40%) at forty minutes and in seven participants at (17.5%) at fifty minutes, that make mean maximum cycloplegic effect occurred between thirty to forty minutes. In compare to R2 where the maximum cycloplegic effect (R2max) in twenty participants (50%) occurred at thirty minutes, fifteen precipitants (37.5%) at forty minutes and only in five precipitants (12.5%) at fifty minutes. make a shift to maximum cycloplegic time toward the thirty minute (as compared to R1 group:42.5% to 50 minute) which was achieved only after twice application of the eye drops (Table 2).

Table 2: R1 max and R2 max at different times.

	30 min	40 min	50 min
R1max	17 (42%)	16 (40%)	7 (17%)
R2max	20 (50)	15(37.5%)	5 (12.5%)

Decreasing the frequency of eye drops application and shorting duration of whole process without effect on maximum cycloplegia.

CONCLUSION

The combination of 1% tropicamide with 1% cyclopentolate regimen can be shorting the duration required for maximum cycloplegia in mild to moderate refractive error in children in compare to cyclopentolate alone in medium and dark pigmented skin, which is time preserving with effective clinical cycloplegic refraction.

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