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Cyclоplegic Refraction in Children with Cyclopentolate versus Atropine

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Abstract

Background: The ideal cycloplegic drug that is safe, effective and convenient in children is not yet available. This study aimed to evaluate the safety and efficacy of two cycloplegic regimens in hyperopic children. The responses to cycloplegia in different age groups and presence of strabismus were also compared.

Methods: It is the first study done in our country, atropine eye drops 1% (regimen I) and cyclopentolate eye drops 1% (regimen II) was evaluated in fifty children. Cycloplegic refractions were assessed.

Statistical analysis: The data are presented as mean and standard deviation (SD). Statistical analysis was performed using the SPSS software 17. A P-value of less than 0.05 was considered statistically significant.

Results: The total refractions were recorded after cycloplegia with atropine 1% or cyclopentolate 1% eye drops. Atropine refraction (mean+3.89 ± 2.45 D) was statically insignificantly comparing with cyclopentolate refraction (mean +3.58 ± 2.30 D; P>*0.05*

Conclusion: We suggest that the cyclopentolate applied to younger or older children is sufficient to produce good cycloplegia, with an effect similar to atropine.

Keywords: Cyclopentolate; Atropine; Hyperopia; Children

Introduction

The refracting power of the eye results from the static power of the eye (the combined ability of the cornea and the lens to bend incoming rays of light) and the accommodative power of the eye (the variable force of accommodation that alters the path of light rays by causing the ciliary body to change the curvature of the lens). The total increase in plus power that accommodation produces is known as, the amplitude of accommodation [1].

The ciliary body in humans contains muscarinic receptors in the parasympathetically innervated smooth muscle fibers [2]. The presence of adrenoceptors has also been described [3].

Cycloplegia inhibits the accommodative power of the eye by blocking the action of the ciliary muscle, allowing the static or objective refractive error of the eye to be measured. The best way to obtain paralysis of accommodation is to use cycloplegic drugs. Cycloplegic drugs are called anticholinergic because they block the muscarinic action of acetylcholine. This action inhibits cholinergic stimulation of the iris sphincter and ciliary muscle, which results in mydriasis and cycloplegia [1].

Cycloplegic refraction is invaluable in the evaluation of patients with decreased vision or ocular deviation. The rationale for cycloplegic refraction is that patients have different levels of accommodation at different times [4].

Cycloplegic examinations not only allow refractive error to be determined, they also dilate the pupil, preparing the patient for an ophthalmoscopic examination. All children require a thorough ophthalmoscopic examination, which enables the physician to look for opacities in the ocular media and abnormalities in the inner eye [1].

Cycloplegic refraction helps determine full hyperopia in patients with accommodative esotropia and prevents overcorrection in myopic patients. It is also useful in prescribing correction in patients with limited cooperation during subjective refraction and amblyopic patients who have chaotic accommodation [4,5].

The indications for cycloplegic refraction are limited in adults. As amplitude of accommodation gradually decreases with age, a closer agreement between cycloplegic and manifest refraction findings takes place. The 17 diopters of accommodation of a 3-year-old child decreases to 14 diopters at 10 years of age, 10 diopters at 25 years of age, 6 diopters at 40 years of age, and 2 diopters or less at age of 50. Cycloplegia may be necessary in handicapped or mentally disabled individuals because of their unresponsiveness to subjective refraction; it also may be used to objectively evaluate the suspected malingerer or hysteric. Young adults with asthenopic symptoms who use their accommodation to compensate for their hyperopic refractive error may require a cycloplegic examination when the manifest refraction reveals too little hyperopia to account for their symptoms. Blurred vision or headaches after sustained reading or changing focus from near to far may be caused by latent hyperopia. With the advent of modern laser refractive surgery, cycloplegic refraction has become a valuable preoperative test for accurately determining refractive error [1].

In older children and young adults, cycloplegic refraction can confirm the diagnosis of accommodative spasm, which is a constant or intermittent, involuntary increase in ciliary contraction. Ciliary spasm may be caused by spasm of the near reflex or high ciliary tonus, or secondary to factors such as hyperopia or convergence insufficiency. Patients with low hyperopia may present as myopic during examination; this so-called pseudo myopia can be identified by cycloplegic evaluation [1].

The two most commonly used cycloplegic drugs, atropine and

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cyclopentolate, act by competing with the physiological muscarinic agent acetylcholine, resulting in inhibition of ciliary muscle contraction. Atropine may also have a partial μ -agonist effect [6]. Numerous studies have documented the comparative efficacy of these cycloplegic drugs [7-12]. However, there is no clear consensus as to the ideal cycloplegic drug. Comparisons of combinations of these drugs have also failed to indicate the ideal regimen [13-15]. Possible reasons for the variable results could be the differences in drug combinations, treatment regimens and patient populations.

The two drugs routinely used for cycloplegic refraction include atropine and cyclopentolate. Atropine is the gold standard for complete cycloplegia but it needs at least 3 hours to reach peak effect and must be used for 3 days to produce complete cycloplegia. It takes 8–14 days for its effect to wash out from the pupil and ciliary body.

Atropine may lead to complications such as fever, tachycardia, convulsions, and even death, and is contraindicated in patients with Down syndrome and albinism [16]. On the other hand, cyclopentolate has a faster onset of effect and reaches peak effect after 30–45 minutes; its cycloplegic effect washes out after 6–8 hours. It incurs fewer complications and has become the drug of choice for cycloplegia [17].

The toxic effects of atropine may be summarized by the saying: 'as blind as a bat, dry as a bone, red as a beetroot and mad as a hatter'. Patients are 'blind' owing to the induced cycloplegia, 'dry' due to the inhibition of the sweat and salivary glands (one of the first signs of atropine poisoning is a dry mouth), 'red' because of peripheral vasodilation (produced in an attempt to lose heat and to overcome the lack of function of the sweat glands) and 'mad' owing to effects on the central nervous system (CNS) [18].

The adverse effects of cyclopentolate are generally divided into those of an ocular and systemic nature. Almost all ocular drugs have undesirable side-effects, although according to Rengstorff and Doughty' the complications from mydriatic and cycloplegic drugs are rare compared with their extensive use [19].

Some authors have shown no significant difference between the cycloplegic effect of cyclopentolate and atropine [20,21]. Inadequate cycloplegia can cause inaccurate refraction and lead to inappropriate diagnostic and therapeutic approaches; on the other hand, over dosage of cycloplegics may cause drug reactions or lead to undue patient discomfort. The unpleasant nature of instilling eye drops especially in children can prevent completion of the examination and is so important that sprays have been suggested instead of eye drops by some authors [22].

The younger the patient, the greater the patient's amplitude of accommodation and the more difficult it is to inhibit it. Because of the powerful accommodation and the inability of young pediatric patients to respond with accurate subjective responses, cycloplegic refraction rather than manifest or subjective refraction usually is necessary. In older children and adults, noncycloplegic methods of inhibiting accommodation, such as fogging, become more practical clinically, but cycloplegics can be used selectively to help determine the refractive state of the eye [1].

Cycloplegia allows estimation of true refractive error by relaxing accommodation [1]. Most clinicians; however, agree that cycloplegia is necessary when performing refraction in young children, high hyperopia, and patients with strabismus [23]. The ideal cycloplegic drug that is safe, effective and convenient allowing accurate measurement of the dioptric error by both subjective and objective means is not yet available.

Cycloplegia is necessary for controlling accommodation and obtaining an accurate refraction in young children. No other technique, such as fogging, can replace cycloplegia for preciseness in determining refractive errors in early childhood because it does not depend on patient cooperation or fixation distance [1].

It is universally accepted that refraction in children, irrespective presence or absence of strabismus and type of refractive error, should preferably be performed under cycloplegia [4].

Cycloplegic refraction should be done routinely in the pediatric age group, especially in patients with esodeviation [24]. Atropine, the strongest cycloplegic known, used frequently in children, has its own disadvantage in the form of prolonged action [25]. Cyclopentolate hydrochloride, another parasympatholytic drug, is perhaps the most commonly used cycloplegic in children [4].

Most clinicians, however, agree that cycloplegia is necessary when performing refraction in young children, high hyperopia, and patients with strabismus [8]. Several investigators have shown atropine to be more effective than cyclopentolate in blocking accommodation in young esotropic children [14].

The entire hypermetropic refractive error is usually prescribed in the spectacle correction of children with esotropia who are less than 5 years of age. Complete blockade of the ciliary hypertonus is necessary to eliminate all accommodation-induced convergence. If adjustment to the full hypermetropic correction is not prompt, a short course of a cycloplegic drug such as atropine is useful. The key to determining the full hypermetropic correction is a proper cycloplegic refraction, repeated one or two times several months apart. In most cases of esotropia with hypermetropia in children less than 5 years of age, atropine or scopolamine preferably is used to ensure that no residual accommodation goes unrecognized [1].

Although indicated for all patients with ocular motility disorders, cycloplegic refraction is indispensable to the clinician in diagnosing and managing accommodative vergence anomalies. The role of accommodation in esotropia is well recognized. A fully accommodative deviation exists when no tropia is present after accommodation is fully relaxed. Most esotropic vergence disorders are partly accommodative and are characterized by an abnormal accommodative-convergence ratio. Treatment includes blocking accommodation by the use of plus lenses and miotics [1].

Cycloplegia can be used in pharmacologic occlusion therapy when the nonamblyopic eye is sufficiently hypermetropic that effective blurring of vision can be obtained by instilling a cycloplegic drug in that eye alone. The success of this penalization therapy can be determined in the office by blurring the sound eye with a short-acting cycloplegic agent, removing the spectacle correction, and evaluating the fixation preference. If under test conditions the patient switches from using the good eye to using the amblyopic eye, chances are excellent that he or she will also do so during treatment and that penalization will force the amblyopic eye to be used [1].

Aim of the Study

To evaluate the cycloplegic effect of cyclopentolate 1% compared with atropine in children with hyperopia.

Patients and methods

Fifty children between the ages of (3 - 8 years), with hyperopia of more than 1.00 D in at least one eye, were enrolled consecutively in

a prospective fashion among patients attending the outpatient clinic. Twenty eight of them were males and the others were females. Exclusion criteria included known cardiovascular disease, ophthalmic disease other than refractive error and/or strabismus, history of allergy to atropine or cyclopentolate, and inability to comply with the treatment regimen. All children underwent a routine ophthalmic evaluation.

Regimen 1 was consisted of instillation of atropine 1% eye drop twice daily for 3 days prior to and on the day of examination. After application of drops, the lacrimal puncti were occluded by pressure on the medial canthus for 3 minutes, to minimize systemic absorption. Parents were informed about the signs of local and systemic toxicity due to the drugs used and they were instructed to return the children to the clinic if adverse events were noted.

Regimen II was consisted of instillation of cyclopentolate 1% eye drops instilled in the conjunctival sac two times at intervals of 5 minutes on the day of examination, refraction was performed 30 min after last drop by mean of retinoscopy.

Post-instillation side-effects were ascertained during follow-up. The refraction was expressed as spherical equivalent (SE) refraction, which was calculated as sphere plus half of the cylinder. The data are presented as mean and standard deviation (SD). Statistical analysis was performed using the SPSS software 17. A P-value of less than 0.05 was considered statistically significant. The study and data collection conformed to all local laws and were compliant with the principles of the Declaration of Helsinki (JAMA 1997; 277: 925-926).

Results

As shown in table 1 below, a total of 50 children (100 eyes) with a mean ± SD age of (4.53 ± 1.31years) range (3–8 years) were enrolled prospectively. The total refractions were recorded after cycloplegia with atropine 1% (regimen 1) or cyclopentolate 1% (regimen ll). Atropine (mean +3.89 ± 2.45 D) was statically insignificant in comparison with cyclopentolate (mean +3.58 ± 2.30 D; P <0.05).

No serious adverse event was reported for any child using the two regimens. Children were divided into two groups according to age of (5 years) old, either younger or older than (5 years). In younger children, the cycloplegic refractions after atropine (mean +4.10 ± 2.91 D) followed by cyclopentolate (mean +3.70 ± 2.73 D; P <0.05). In children older than 5 years of age, atropine (mean +3.62 ± 1.67 D) followed by cyclopentolate (mean +3.42 ± 1.62 D; P >0.05).

Discussion

Full cycloplegia is a basic procedure in the diagnosis and treatment of a number of important ophthalmic disorders, particularly in children who are at the critical age of visual maturation and have higher amplitudes of accommodation acting as an obstacle against accurate refraction. The ideal cycloplegic agent should produce complete cycloplegia with minimal complications or morbidity and allow rapid recovery of accommodation.

Characteristics of the ideal cycloplegic agent include rapid onset of action, quick recovery of normal accommodative function, sufficient cycloplegia and no local or systemic side-effects [26]. None of the currently available drugs fulfill all of these criteria [27], many authors consider atropine as the drug of choice for complete cycloplegia and believe that cyclopentolate cannot be an appropriate substitute [15,28].

Generally it is necessary to use long-acting atropine at home for three days in order to obtain complete cycloplegia. However, the

Pt.no.	Age(years)	Atropine1% (regimen 1) Rt / Lt eye	Cyclopentolate1% (regimen 2) Rt /Lt eye	Differ.(S)
1	4.00	+2.50	+2.25	0.25
		+2.50	+2.00	0.50
2	3.00	+3.00	+2.50	0.50
		+3.00	+2.50	0.50
3	3.50	+2.50	+2.25	0.25
		+2.50	+2.00	0.50
4	3.00	+2.50	+2.25	0.25
		+2.50	+2.25	0.25
5	4.00	+3.50	+3.25	0.25
		+3.50	+3.25	0.25
6	3.50	+4.00	+3.75	0.25
		+4.00	+3.75	0.25
7	3.00	+1.50	+1.50	0.00
		+1.50	+1.50	0.00
8	4.00	+1.50	+1.00	0.50
		+1.50	+1.25	0.25
9	5.50	+4.50	+4.25	0.25
		+4.00	+3.75	0.25
10	3.00	+4.00	+3.50	0.50
		+4.00	+3.50	0.50
11	3.50	+6.50	+6.25	0.25
		+6.50	+6.25	0.25
12	5.50	+5.00	+4.75	0.25
		+5.00	+4.50	0.50
13	6.00	+4.00	+3.75	0.25
		+4.00	+3.75	0.25
14	3.00	+2.50	+2.25	0.25
		+2.50	+2.25	0.25
15	6.00	+2.50	+2.25	0.25
		+2.50	+2.25	0.25
16	5.00	+1.25	+1.00	0.25
		+1.25	+1.00	0.25
17	4.00	+3.50	+3.25	0.25
		+3.50	+3.25	0.25
18	6.50	+2.50	+2.50	0.00
		+2.50	+2.50	0.00
19	4.00	+2.50	+2.00	0.25
		+2.50	+2.00	0.50
20	7.00	+2.75	+2.75	0.00
		+2.75	+2.75	0.00
21	8.00	+6.00	+6.00	0.00
		+6.00	+6.00	0.00
22	3.50	+2.50	+2.50	0.00
		+2.50	+2.50	0.00
23	4.00	+5.00	+4.50	0.50
		+5.00	+4.50	0.50
24	3.00	+4.00	+3.50	0.50
		+4.00	+3.50	0.50
25	4.00	+6.00	+5.00	1.00
		+6.00	+5.00	1.00
26	3.00	+4.00	+3.75	0.25
		+4.50	+4.25	0.25
27	4.00	+3.50	+3.25	0.25
		+3.50	+3.25	0.25
28	3.00	+4.00	+3.50	0.50
		+4.00	+3.50	0.50
29	4.00	+8.00	+7.00	1.00
		+8.00	+7.00	1.00
30	5.50	+1.00	+1.00	0.00

		+2.00	+2.00	0.00
31	2.50	+3.50	+3.00	0.50
		+3.50	+3.00	0.50
32	4.50	+4.00	+3.75	0.25
		+4.00	+3.75	0.25
33	5.00	+3.25	+3.25	0.00
		+3.25	+3.25	0.00
34	5.00	+3.00	+3.00	0.00
		+3.50	+3.25	0.25
35	5.00	+3.25	+3.00	0.25
		+3.25	+3.00	0.25
36	6.00	+5.00	+4.50	0.50
		+5.00	+4.50	0.50
37	6.00	+4.50	+4.00	0.50
		+5.00	+4.50	0.50
38	8.00	+3.00	+2.75	0.25
		+3.00	+2.50	0.50
39	5.00	+3.50	+3.00	0.50
		+3.50	+3.00	0.50
40	5.00	+1.00	+1.00	0.00
		+1.00	+1.00	0.00
41	5.50	+4.50	+4.25	0.25
		+5.50	+5.00	0.00
42	5.00	+2.50	+2.50	0.00
		+2.50	+2.50	0.00
43	5.50	+3.00	+2.75	0.25
		+3.00	+2.75	0.25
44	6.00	+4.00	+4.00	0.00
		+4.00	+4.00	0.00
45	3.00	+1.50	+1.50	0.00
		+1.50	+1.50	0.00
46	5.00	+8.50	+8.00	0.50
		+8.50	+8.50	0.00
47	4.00	+4.00	+3.25	0.75
		+4.00	+3.25	0.75
48	3.00	+17.00	+16.00	1.00
		+17.00	+16.00	1.00
49	4.50	+5.25	+4.75	0.50
		+5.25	+4.75	0.50
50	4.00	+2.50	+2.50	0.00
		+2.50	+2.50	0.00

Pt.no. : patient number, Rt/Lt eye: right/left eye

Table 1: age, cycloplegic refraction with atropine, cyclopentolate eye drops and the difference between two refractions.

parents often have difficulties in applying the drops in a correct manner and doubts often arise whether a full cycloplegic effect has been achieved. Moreover, a prolonged cycloplegia during a sensitive period might, in some cases, potentiate stimulus deprivation and contribute to amblyopia (Ikeda & Tremain1978) [29].

Atropine is the gold standard for producing cycloplegia; however, due to its complications, the difficult regimen, and prolonged impairment of near vision, has gradually been replaced by cyclopentolate, which has less complications, easier to administer, and has a shorter duration of action. Many authors have demonstrated that the cycloplegic effect of cyclopentolate is comparable to atropine [20,21,30]. Others believe that cyclopentolate alone is not enough in children 2 to 5 years old, especially in esotropic children with hyperopia greater than (2 Diopters) who must be repeatedly refracted with atropine to detect latent hyperopia [9,31].

Various products combining different combinations and concentration of cycloplegic agents have been prepared to achieve complete cycloplegia and at the same time avoid the complications and morbidity of atropine [13,32,33].

In a survey to evaluate the incidence of adverse effects for the use of diagnostic pharmaceutical agents, the incidence of adverse events was only 0.2% [34]. However, the researchers included a wide range of dilating eye drops from mild to strong agents, In addition, significant side-effects have also been reported, including tachycardia, tremor and delirium [35,36]. As a result, although atropine provides adequate cycloplegia, the prolonged duration of action and side-effects have prompted a search for alternate cycloplegic agents [35].

In this study, a comparison has been made between the routine instillation of atropine at home by the parents with the instillation of cyclopentolate administered at the hospital. The two drugs in this study appear remarkably similar, even in children with a high degree of hypermetropia.

Cyclopentolate does not produce a complete cycloplegia (Ingram & Barr 1979) [28], particularly in children with a high degree of hypermetropia Rosenbaum et al. 1981 [9], found that 22% of the children in their study had an additional hyperopia of (+1.0) dioptre or more which was uncovered by atropine.

The synthetic antimuscarinic (parasympatholytic) drug, cyclopentolate, has a shorter duration of action. The maximum cycloplegic effect is attained after 45 minutes, and remains stable for 90 min [14]. Therefore; we evaluated this versus atropine in eyes of children in this study.

However, central nervous system toxicity including mental deterioration and grand mal seizure can occur with cyclopentolate [37,38]. No adverse effects were recorded and this may be explained by small sample size used.

The results of the present study have clinical importance as there are many disadvantages with atropinisation at home. Compliance is often unsatisfactory, the drug effects are long-acting, and it is often difficult to decide whether a complete cycloplegic effect has been achieved. The instillation of a short-acting cyclopentolate drop by trained personnel at the time of examination offers many advantages. The present results suggest that it is possible to replace atropinisation at home with the instillation of cyclopentolate in the hospital.

Observations of this study conclude that 2 drops of 1% cyclopentolate hydrochloride, 5 minutes apart, provide considerable cycloplegia sufficient for refraction in most children [39]. Cyclopentolate can be safely used for refraction in children, but precaution should be taken as it tends to be less cycloplegic in young children with high hypermetropia and is also known to exhibit anisocycloplegia, a queer phenomenon described by Beach [40]. The parents of the child should also be instructed about the transient acute psychosis which may occasionally occur even with few instillations at low concentrations [41]. However, atropine, a proven effective cycloplegic drug, should be reserved for children (less than 6 years) with a large amount of accommodative esotropia and those with history of cyclopentolate induced psychosis.

Concerning cycloplegic effect; in children younger than (5) years old, the cycloplegic refractions after atropine (mean +4.10 ± 2.91 D) followed by cyclopentolate (mean +3.70 ± 2.73 D; $P < 0.05$). In older children, atropine (mean +3.62 ± 1.67 D) followed by cyclopentolate (mean +3.42 ± 1.62 D; $P > 0.05$). There were only six eyes, all of them younger than 5 years of age that had 1.00 D hyperopia uncovered by atropine but not by cyclopentolate.

Robb and Peterson found that atropine uncovered (0.3–0.4 D) more hyperopia than cyclopentolate in children younger than 6 years old [42]. In contrast, Rosenbaum studied white esotropic children younger than 5 years with cyclopentolate and atropine, and showed that atropine was probably unnecessary [9].

For cycloplegic refraction, an allowance (under correction) has to be made for abolished ciliary tone and this tonus allowance is taken as 1.0 dioptre in the case of atropine [43]. Gettes [44] recommended an equal tonus allowance for both cyclopentolate and atropine; while, on the other hand, Davies (1981) suggested that a tonus allowance for cyclopentolate or any other cycloplegic for that matter, with the exception of atropine, is inappropriate.

Previous studies have used a reduced concentration of atropine in younger children [12,35,45]. This appeared paradoxical because younger children have a greater accommodative response [8]. The possible reason for this strategy was to reduce the incidence of atropine toxicity in younger children.

This study included children older than 3 years and none of the children had any side-effects due to atropine use. Thus, although the sample size was limited and the number of installations differed in different regimens, the study indicates the safety and efficacy of atropine 1% in this population.

The importance of atropine cycloplegia in the evaluation of strabismic children has been stressed in earlier reports [8,46]. The study showed that children with or without strabismus, cycloplegic refraction after atropine and cyclopentolate not show a statistically significant difference. Thus, cyclopentolate might be considered as the choice for cycloplegic refraction for children with or without strabismus.

Conclusion

Atropine is the gold standard for producing cycloplegia; however, due to its complications, difficult regimen and prolonged impairment of near vision, it has gradually been replaced by cyclopentolate, which has less complications, easier to administer, and has a shorter duration of action.

This study found a good correlation between atropine and cyclopentolate and the two regimens appear remarkably similar, even in children with a high degree of hypermetropia.

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