

Side effects of 1% cyclopentolate hydrochloride in children and adolescents attended at Centro Universitário FMABC

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ABSTRACT

Introduction: It is known that vision disorders are within the context of public health problems. In childhood, during the neuropsychomotor development phase, visual changes are crucial, since there is a strong correlation between poor school performance and changes in acuity. For these reasons, ophthalmological examination in children, including refraction, is extremely important, aiming at the early diagnosis of diseases and possible refractive errors that may compromise the child's life and development. 1% cyclopentolate hydrochloride eye drops are the most used during ophthalmic clinical evaluation as a cycloplegic and mydriatic agent to assist in refractive examination. **Objective:** The ocular and systemic side effects of 1% cyclopentolate hydrochloride eye drops were studied in patients who underwent static refractive examination in the strabismus sector of the Ophthalmology Discipline of the Centro Universitário FMABC. **Methods:** A drop of 1% cyclopentolate is instilled in both eyes of each patient and the possible ocular and systemic signs and symptoms presented were observed after 40 minutes and 24 hours after instillation. **Results:** we expect to find ocular side effects more evident than systemic symptoms in the two evaluation times (40 minutes and 24 hours after instillation). All symptoms (ocular and systemic) are reversed spontaneously. **Conclusion:** The present study aims to show that the side effects observed by the topical (ocular) use of cyclopentolate eye drops 1% are few and present spontaneous reversal both from an eye point of view, as well as from a systemic point of view.

Keywords: cyclopentolate hydrochloride; side effects; cyclopegia.

INTRODUCTION

Vision disorders are within the context of public health problems. In childhood, during the neuropsychomotor development phase, visual changes are crucial, since there is a strong correlation between poor school performance and changes in acuity¹. Vision is responsible for most of the sensory information we receive from the outside world,

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being extremely important for learning. The World Health Organization (WHO) estimates that 7.5 million school-age children have some type of visual impairment and only 25% of them have symptoms; others $\frac{3}{4}$ would need specific testing to identify the problem².

Gianini et al.³, described that international studies estimate that approximately 25% of school-age children have some type of visual impairment. In Brazil, according to the Brazilian Council of Ophthalmology (BCO), these numbers are close to 20%.

For these reasons, ophthalmological examination in children, including refraction, is extremely important, aiming at early diagnosis of diseases and possible refractive errors that may compromise the child's life and development. Routine eye examination includes the use of cycloplegic eye drops. In children, due to its high accommodative capacity, the use of this medication is essential for the correct prescription of refraction. Cyclopentolate hydrochloride eye drops 1% is the most used during ophthalmic clinical evaluation as a cycloplegic and mydriatic agent to aid in refractive examination⁴.

Cyclopentolate hydrochloride is an anticholinergic agent, which blocks the response of the iris sphincter muscles and the ciliary body to cholinergic stimulation, producing pupillary dilation (mydriasis) and accommodation paralysis (cycloplegia)⁵. The route of administration is topical, but its side effects can be observed both locally (ophthalmological) and systemic. The therapeutic and adverse effects of this are due to its connection with muscarinic receptors in a target organ⁶. After application, the maximum effect occurs in 30 to 60 minutes and the total recovery of visual accommodation normally occurs between 6 and 24 hours⁷.

When compared to atropine (another medication that has already been used a lot for routine eye examination), cyclopentolate hydrochloride 1% has moderate and short-lasting side effects⁸. Its side effects have a higher dose-dependent relationship with the use of eye drops than with the particular characteristics of each patient⁹.

The present study aims to observe the signs and symptoms present after instillation of 1% cyclopentolate hydrochloride eye drops in both eyes (two doses) in patients undergoing refractive examination (static refraction) in the strabismus sector of the Discipline of Ophthalmology from Centro Universitário FMABC.

METHODS

Study Design and Patients

This is a prospective study that evaluated the systemic and ophthalmological effects of cyclopentolate 1% in healthy children and adolescents from 6 to 17 years old, this drug is used

for the purposes of cycloplegia and mydriasis in the ophthalmological clinic. All participants were attended at the ABC Medical School outpatient clinic from September 2019 to November 2019, and signed the Free and Informed Consent and Consent Form (TCALE) with the acceptance to participate in the study. This study was submitted for analysis by the Ethics and Research Committee of the Centro Universitário FMABC. The patients submitted to the study were informed about the possible side effects predicted in the medication leaflet, the main ones being: visual haze close up, photophobia, mydriasis (dilation of the pupil) and systemic effects such as headache, drowsiness, nausea, dry skin, fever, facial flushing, tachycardia, dry mouth, headache, dizziness, among others.

The administration of cyclopentolate hydrochloride 1% was performed via the eye and after 40 minutes of administration, patients were asked about the possible side effects of the eye drops. All patients underwent refractive examination 40 minutes after the second dose, which consisted of applying a drop of 1% cyclopentolate hydrochloride to each eye every 5 minutes in 2 doses.

40 minutes after instillation of the first drop of medication in both eyes, the patient answered a questionnaire related to the ocular and systemic symptoms observed in this period.

24 hours after the exam, the patient was again asked by phone about the duration of the medication's effects (whether there was spontaneous remission or if any symptoms still persisted).

The inclusion criteria for participation in the research are: 1) patients treated at strabismus outpatients aged over 6 years and under 18 years. The exclusion criteria are: 1) patients who are known to have a history of allergy to any component of the medication. 2) under 6 years old and over 18 years old. 3) patients who for some reason were unable to apply the second drop of medication exactly 5 minutes after the first. 4) patients who were not present for reassessment exactly 40 minutes after instillation of the first drop. 5) patients who were unable to contact 24 hours after the first exam to answer about the effects of medication. 6) patients who voluntarily dropped out of the study.

RESULTS

The present study analyzed 18 children and adolescents with a minimum age of 6 years and a maximum age of 17 years and 11 incomplete months. The average age of patients is 10 ± 3 years and four months upwards or downwards. Regarding gender, 44.4% of the sample studied are female and the rest (55.6%) are male (Table 1).

Five groups of possible manifestations of medication-related side effects (cyclopentolate hydrochloride 1%) were evaluated 40 min after the first drop was applied and 24 hours after the eye examination. These groups are:

1. Ocular manifestations: (mydriasis, conjunctival hyperemia, photophobia, eye pain, burning, itching, near-visual blurring, visual blurring).
2. Adrenergic manifestations: (facial flushing, fever, dry skin, dry mouth, tachycardia, peripheral vasodilation).
3. Neurobehavioral manifestations: (drowsiness, crying, fatigue, restlessness, joy; animation, loud laughter, vertigo, dizziness, nausea, fear, headache, visual hallucinations, tactile hallucinations, altered voice intensity, disorientation in time, space, speech disconnected and meaningless, non-recognition of people and objects, recent memory deficit, change in sexual behavior, change in gait, limb paresthesias, generalized seizure).
4. Allergic manifestations: (periorbital hyperemia, periorbital edema, urticarial rash, anaphylactic shock).
5. Gastrointestinal manifestations: (food intolerance, vomiting, abdominal distention).

Ocular manifestations were the most cited in the group of patients studied 40 minutes after the medication was instilled and 24 hours after the exam.

Table 1: Characteristics of patients

Parameters	
Age (years)	10±3.4
Sex	
Women	44.4%
Male	55.5%

62.5% of complaints after 40 minutes were related to some ophthalmological symptom, with 100% of patients claiming visual haze close by, 77% presented mydriasis followed by 27.7% with visual haze and 11.1% with ocular pain.

37.5% of complaints 40 minutes after instillation of cyclopentolate eye drops 1% were related to neurobehavioral manifestations, with the 3 symptoms mentioned among the participants: somnolence, nausea and headache. The three complaints correspond to 37.5% of all complaints and represent 5.5% each (presented in only 1 patient in the study) (Figure 1).

There were no complaints of adrenergic or gastrointestinal manifestations in the public studied. Side effects showed spontaneous remission and treatment was not necessary to improve them. After 24 hours of the eye examination, 55.5% of the patients were asymptomatic.

As it is an anticholinergic substance, we evaluated the studied group as to the possible effects of changes in heart rate 40 minutes after instillation of cyclopentolate 1%. According to the medication instructions, it is in this period (between 30 and 60 minutes) that 1% cyclopentolate applied topically to the eyes reaches its maximum ophthalmological effect.

Figure 2 shows that there was no significant variation in heart rate in the patients analyzed. The mean heart rate (HR) of patients before instillation of the medication was 90.5 beats per minute (bpm) with a standard deviation of 31.36 bpm. After 40 minutes, the patients' mean heart rate was 83.72 bpm with a standard deviation of 21.49 bpm.

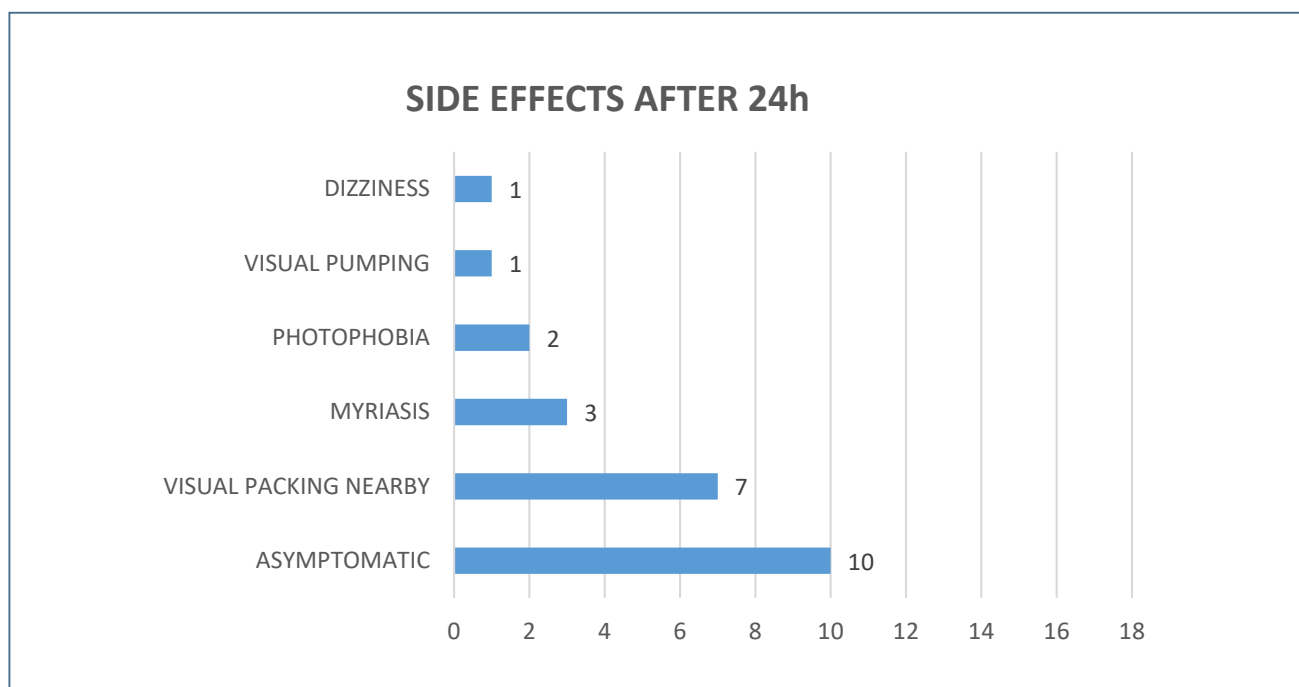


Figure 1: Side effects after 24 hours of administration of cyclopentolate 1%.

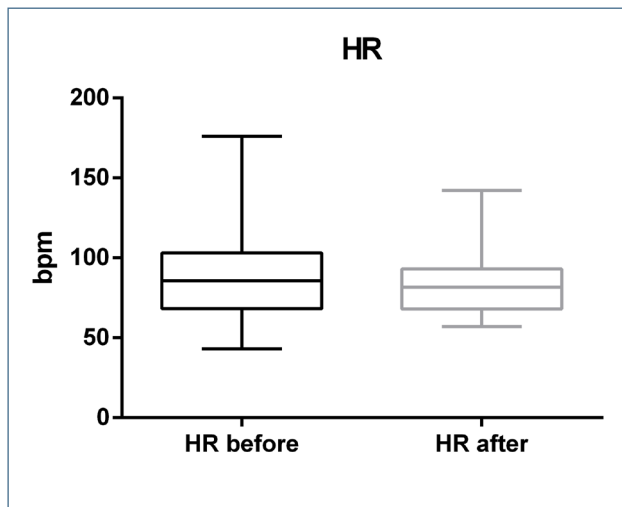


Figure 2: Graphical representation of the heart rate (HR) data of the patients in the study. Student T test.

DISCUSSION

Cycloplegia for refractive examination has been used for many years in ophthalmic practice. However, in the past the most used eye drops were atropine. This, due to its longer-lasting side effects and cycloplegics, was being replaced by cyclopentolate hydrochloride 1% in the early 1950s. Cyclopentolate is an anticholinergic agent, which blocks the response of the iris sphincter muscles and the ciliary body to cholinergic stimulation, producing pupillary dilation (mydriasis) and paralysis of accommodation (cycloplegia)¹⁰.

The ideal characteristics of a cycloplegic would be a rapid onset of action, severe depression of accommodation, followed by its rapid recovery with few or no side effects¹¹. Following this reasoning, cyclopentolate hydrochloride 1% gained space in the

ophthalmologic routine for presenting these characteristics when compared with other cycloplegic agents used until then (ex: atropine) in a study with more than 3,000 participants¹⁰.

Systemic absorption of 1% cyclopentolate hydrochloride occurs transconjunctivally, followed by the passage of the measurement through the nasolacrimal duct, nasal mucosa and gastrointestinal tract¹².

The most described reactions are the manifestations that affect the central nervous system (CNS), the main ones being: headache, visual hallucinations, auditory hallucinations, disorientation, generalized seizure, sedation¹³.

In the present study, the evaluated patients presented mild neurological manifestations (drowsiness, headache, dizziness and nausea) and with spontaneous remission.

The ocular effects were the most prevalent in this study, mainly visual haze for distance, visual haze for near, mydriasis and photophobia. These effects are expected due to the anticholinergic action with antimuscarinic effect on the ciliary muscle and iris sphincter.

Allergic reactions (urticarial rash on limbs and face and contact dermatitis), as well as gastrointestinal reactions, anaphylaxis and anticholinergic toxicity are described in some studies as rare and were not reported by the patients in this study^{12,14,15}.

Conclusion

Cyclopentolate hydrochloride 1% proved to be a safe medication, presenting tolerable side effects with spontaneous remission proving its safety in the use of routine ophthalmic clinical practice. Excessive medication instillations should be avoided. In the present study, the dose studied (1%) and frequency of application (2 drops in both eyes within a 5-minute interval between them) proved to be safe for the group of patients studied.

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