

Systemic Toxicity of Topical Cyclopentolate Ophthalmic Solution in a Child

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ABSTRACT Cyclopentolate hydrochloride (CH) is a topical agent used in ophthalmological examinations for mydriasis whose both ocular and systemic side effects can occur after administration. In children, the risk of intoxication increases depending on many risk factors such as smaller body mass index or being severely ill. After the administration of CH ophthalmic solution in the ophthalmology outpatient clinic, an 8-year-old patient with complaints of speaking difficulties and flushing was admitted to the pediatric emergency department. Tachycardia, bilateral mydriasis, and dysarthria were detected and she was diagnosed with the anticholinergic syndrome. Neurological findings improved after 3 hours and mydriasis after 30 hours. It should be taken into consideration that systemic effects may occur as a result of cyclopentolate topical drug application, especially in children, even at an appropriate dose.

Keywords: Child; cyclopentolate; ophthalmic solutions; toxicity

Cyclopentolate hydrochloride (CH) is a cycloplegic and mydriatic agent frequently used in children's ophthalmologic examinations. The mydriatic and cycloplegic effects of cyclopentolate appear within 30-60 minutes after administration and may last up to 24 hours.¹ Although CH eye solutions are absorbed through the conjunctiva and nasolacrimal ducts and cause local effects, sometimes adverse systemic symptoms may also be seen.²

Several reports presented systemic toxicity following topical application of cyclopentolate ophthalmic solution.³⁻⁵ Anticholinergic intoxication symptoms such as flushing, tachycardia, nutritional intolerance, dizziness, and behavioral changes occur in patients.⁶

Here, a pediatric case is reported with central anticholinergic syndrome after application of CH ophthalmic solution.

CASE REPORT

An 8-year-old girl, who underwent refraction examination in her previous controls, applied to the ophthalmology clinic. She was administered CH (1%) ophthalmic solution, 2 drops in each eye. After 15 minutes, flushing started on her face and she stated that she felt uncomfortable. Half an hour later, she did not recognize her father and complained of seeing some objects that were not there. Her speech was inappropriate and irrelevant. Also her skin, especially her cheeks were extremely red, hot, and dry. She was admitted to the emergency department by her father. Her pulse rate was 120/minute fever: 37.8 °C blood pressure: 95/65 mmHg. Her pupils were dilated and light reflexes could not be obtained while she had flushing in her face. On systemic physical examination, respiratory, cardiovascular, and gastrointestinal findings were normal. No urticaria or rash was de-

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Peer review under responsibility of Türkiye Klinikleri Journal of Case Reports.

Received: 12 Aug 2021

Received in revised form: 13 Dec 2021

Accepted: 20 Dec 2021

Available online: 23 Dec 2021

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tected on skin examination. She was speaking irrelevantly and had dysarthria but no additional neurological finding was observed. She was diagnosed with anticholinergic syndrome and admitted to the pediatric clinic for monitoring. Laboratory analyses were normal. She was started on intravenous fluids and oxygenated using a face mask. At the 3rd hour of admission, her speech and behavioral functions returned to normal. Her pupils were dilated for 30 hours. She was discharged within 48 hours of admission while having a normal physical examination. A written informed consent form for publication of the patient's clinical details was obtained from the father of the patient.

DISCUSSION

Due to its cycloplegic effect, CH ophthalmic solution is commonly preferred in pediatric patients for refraction testing. For ophthalmic examination in patients aged between 3.5 and 20 years, 1% cyclopentolate concentration not only provides sufficient mydriasis but also has fewer side effects compared to high concentrations.⁷ In a case with an acute psychotic reaction that occurred with 1% CH solution application, researchers conducted a chemical analysis and revealed that the CH concentration administered was 1.31%, not %1.⁸ Therefore, even if the appropriate concentration of CH ophthalmic solution is administered, systemic side effects may occur. Cyclopentolate is absorbed through the conjunctiva and nasal mucosa and may cause local side effects such as increased intraocular pressure, lacrimal duct obstruction, and corneal damage.⁵ Although it is not common, systemic side effects may be presented with anticholinergic toxicity symptoms, including skin dryness, flushing, fever, tachycardia, irritability, ataxia, hallucinations, and convulsions.² These anticholinergic effects are the result of blockade of acetylcholine receptors in postganglionic neurons.⁹ Given the smaller body mass in children, the risk of toxicity is higher and increases in children who are severely ill, premature or with Down syndrome.³ Anticholinergic toxicity causes stimulation of the medulla and central nerve system. Usually symptoms such as ataxia, dysarthria, disorientation,

hallucination, euphoria, causeless laughter, agitation, increased motor activity, confusion and delirium are seen at the 1st half-hour of application and continue from 4 to 6 hours without causing permanent damage.⁶ Allergic reactions such as urticarial rash, nausea and wheezing may occur.¹⁰

Applying the lowest effective dose and concentration of CH ophthalmic solution for the examination and massaging the punctum after this can reduce the risk of side effects.¹¹ In addition, selecting a less toxic ophthalmic solution to achieve mydriasis in children may prevent systemic side effects. Tropicamide 0.5% ophthalmic solutions, which provide adequate mydriasis in children and cause less toxicity and side effects, might be preferred for ophthalmic examination.¹² Generally, the anticholinergic symptoms resolve spontaneously but in severe cases, physostigmine, a cholinesterase inhibitor, is required.⁴

In conclusion, although it is considered that the effects of topical drug application are local, it should not be forgotten that ophthalmic solutions may have multisystemic effects by joining the systemic circulation, especially in children.

Authorship Contributions

This study is entirely author's own work and no other author contribution.

Source of Finance

During this study, no financial or spiritual support was received neither from any pharmaceutical company that has a direct connection with the research subject, nor from a company that provides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and /or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

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This study is entirely author's own work and no other author contribution.

REFERENCES

1. Pappano AJ, Katzung BG. Cholinceptor-blocking drugs. In: Katzung B, ed. *Basic and Clinical Pharmacology*. 9th ed. New York: The McGraw-Hill; 2004. p.109-21.
2. van Minderhout HM, Joosse MV, Grootendorst DC, Schalijs-Delfos NE. Adverse reactions following routine anticholinergic eye drops in a paediatric population: an observational cohort study. *BMJ Open*. 2015;5(12):e008798. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
3. Bhatia SS, Vidyashankar C, Sharma RK, Dubey AK. Systemic toxicity with cyclopentolate eye drops. *Indian Pediatr*. 2000;37(3):329-31. [[PubMed](#)]
4. Derinoz O, Emeksiz HC. Use of physostigmine for cyclopentolate overdose in an infant. *Pediatrics*. 2012;130(3):e703-5. [[Crossref](#)] [[PubMed](#)]
5. Ünlü C, Şen B, Devrim S, Öztürk İ, Öner E, Üstün Y, et al. A case of paediatric intoxication due to overdose cyclopentolate ophthalmic solution application. *JAREM*. 2017;7:92-4. [[Crossref](#)]
6. Labetoulle M, Frau E, Le Jeunne C. Systemic adverse effects of topical ocular treatments. *Presse Med*. 2005;34(8):589-95. [[Crossref](#)] [[PubMed](#)]
7. Bagheri A, Givrad S, Yazdani S, Reza Mohebbi M. Optimal dosage of cyclopentolate 1% for complete cycloplegia: a randomized clinical trial. *Eur J Ophthalmol*. 2007;17(3):294-300. [[Crossref](#)] [[PubMed](#)]
8. Huismans H. Intoxikationspsychose nach Cyclopentolat-HCL (Zyklolat) [Acute psychosis after cyclopentolate-HCL (Zyklolat) (author's transl)]. *Klin Monbl Augenheilkd*. 1979;175(1): 100-2. German. [[PubMed](#)]
9. Mirshahi A, Kohnen T. Acute psychotic reaction caused by topical cyclopentolate use for cycloplegic refraction before refractive surgery: case report and review of the literature. *J Cataract Refract Surg*. 2003;29(5):1026-30. [[Crossref](#)] [[PubMed](#)]
10. Tayman C, Mete E, Catal F, Akca H. Anaphylactic reaction due to cyclopentolate in a 4-year-old child. *J Investig Allergol Clin Immunol*. 2010;20(4):347-8. [[PubMed](#)]
11. Pooniya V, Pandey N. Systemic toxicity of topical cyclopentolate eyedrops in a child. *Eye (Lond)*. 2012;26(10):1391-2. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]
12. Major E, Dutson T, Moshirfar M. Cycloplegia in Children: An Optometrist's Perspective. *Clin Optom (Auckl)*. 2020;12:129-33. [[Crossref](#)] [[PubMed](#)] [[PMC](#)]