Suad Al-Sulaimani et al. Saudi J Er Med. 2023;4(1):076-079
https://doi.org/10.24911/SJEMed/72-1664129458

CASE REPORT

Seizure associated with topical cyclopentolate: a case report

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ABSTRACT

Introduction: Cyclopentolate is a widely used mydriatic agent with a rapid onset cycloplegic effect. Systemic toxicity from an ophthalmic application is uncommon.

Case Presentation: We present a case of a 13-year-old girl who presented to the emergency department with a generalized seizure after receiving 1% cyclopentolate for three drops in each eye, over 15 minutes, as instructed by the prescriber. The seizure began 30 minutes after receiving the last dose. We also describe the general presentation, characteristics of affected patients, and management of this adverse drug event. Cyclopentolate systemic toxicity is dose-dependent.

Conclusion: This case highlights the importance of caution when using topical ophthalmic cycloplegics in children.

Keywords: Cyclopentolate 1%, eye drops, cycloplegic, seizure, case report, ophthalmic eye drops, case report.

Introduction

Patients who undergo ophthalmoscopic examination often receive cycloplegic eye drops to facilitate the retina examination [1]. Cyclopentolate eye drops are commonly used for this purpose, and cyclopentolate is a muscarinic receptor antagonist similar to atropine [1]. The onset of action is 30-60 minutes, and the effect lasts up to 24 hours [2]. This medication is absorbed through the conjunctiva and nasal mucosa through the nosocomial duct into the systemic circulation. Systemic absorption also occurs through the oropharynx, digestive system, and skin [1,3]. There are several reports of systemic toxicity after topical application of cyclopentolate eye drops. Seizure is a rare adverse effect but is reported more frequently in children [1]. We present a case of a 13-year-old girl who presented to the emergency department (ED) with a generalized seizure after receiving 1% cyclopentolate, for a total of three drops in each eye, over 15 minutes, as part of a routine ophthalmology examination.

Case Presentation

This case describes a 13-year-old girl with a developmental delay and learning disability. She was born at 40 weeks by cesarean section due to fetal distress and had a birth weight of 3 kg. She performs poorly in school but has no physical disability or prior history of seizures. The patient was reviewed in the ophthalmology clinic for a routine examination during which her pupils were dilated with three drops of 1% cyclopentolate in each eye to facilitate the retinal examination. Thirty minutes after the instillation of the eye drops, the patient had a grand mal seizure that lasted approximately 10 minutes before spontaneous termination. The seizure was described as a generalized seizure with upward rolling of the eyes, jerky movement of the upper and lower extremities, and urine incontinence. The seizure was not preceded by an aura.

She was transferred to the ED of the same hospital in a postictal state. She experienced no additional seizures. On arrival to the ED, her heart rate was 78 beats/minute, her blood pressure was 106/60 mmHg, and her respiratory rate was 18 breaths/minute. Her oxygen saturation was 100% on room air, and she was euglycemic.

On physical examination, we noted somnolence and aphasia. We saw no new focal neurological deficits. The

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Received: 25 September 2022 | **Accepted:** 06 January 2023

patient's pupils remained widely dilated, and there were no other features of atropinization. The other findings of her physical examination were unremarkable.

We obtained a complete metabolic panel in the ED and noted no gross abnormalities (Table 1). Urgent computed tomography imaging of the head showed no abnormalities. An electroencephalogram was performed, and a follow-up appointment was scheduled.

WBC, white blood cells; HGB, hemoglobin; PLT, platelets; AST, aspartate aminotransferase; ALT, alanine transaminase; INR, international normalized ratio; PT, prothrombin time; Cr: creatinine; CRP, C-reactive protein; pCO_2, partial pressure of carbon dioxide; HCO_3, bicarbonate.

The physician caring for the patient consulted the pediatric team, who recommended providing supportive care. The toxicology service was also consulted and recommended an additional study to determine the etiology of the seizure. The toxicology service suggested that the seizures may have been related to cyclopentolate eye drops and advised that the patient should not receive cyclopentolate in the future. The patient's follow-up with the pediatric neurologist as an outpatient was arranged within 2 weeks.

Discussion

Seizures are frightening, worrisome, and relatively common events. Approximately 3%-4% of children in the general population experience at least one convulsion in their lifetime [4]. There are many causes of seizures in children, and idiopathic seizures can reflect drug exposure. This has been estimated to account for 6% of new-onset generalized tonic-clonic seizures in individuals presenting to the ED [4].

An American Association for Pediatric Ophthalmology and Strabismus survey reported five cases of cyclopentolate-induced seizure. The median age was 5 years (range: 3 months to 12 years), and the average time from the instillation of cyclopentolate eye drops to seizures was 12 minutes [4]. Three patients had generalized convulsions, whereas two had focal seizures [5].

Cyclopentolate has been well reported to cause central nervous system (CNS) toxicity manifesting as seizures with as little as one drop in the eye. According to Lahdes et al. [6], plasma concentrations of cyclopentolate eye drops become notable within 30 minutes of installation. Occasionally, a second concentration peak in plasma is seen after 2 hours. They reported that the mean elimination half-life was 111 minutes, with no significant differences between the formulations concerning the time course of plasma drug concentration [6].

Different factors might increase the risk of adverse effects of cyclopentolate in infants and young children. The risk of toxicity is greater with higher concentrations and frequency of administration. Immaturity and neurological disorders could predispose children to increased sensitivity to the systemic effects of cyclopentolate eye drops [3]. One study reported that a toddler with no history of seizures developed a grand mal seizure for 30 minutes after receiving three drops of 10% phenylephrine and 1% cyclopentolate in each eye every 5 minutes. These seizures occurred 45 minutes after the last dose of each eye drop [1]. A summary of the collective data from previously reported cases in the literature is presented in Table 2.

Our patient's experience supports the theory that immaturity and neurological disorders could predispose a child to increased sensitivity to cyclopentolate toxicity [3], and our patient may have a reduced seizure threshold. Her developmental delay and relatively immature brain may have been the predisposing factors responsible for the CNS toxicity induced by cyclopentolate eye drops. The exact mechanism remains unknown, but neurological disorders may be considered a contraindication for cyclopentolate eye drops, especially in children [3]. Furthermore, although seizures rarely

Table 1. *Laboratory tests.*

Analyte	Patient value	Reference range
WBC (10^3/µl)	7.3	2.4-9.5
HGB (g/dl)	13.8	11-14.5
PLT (10^3/µl)	326	150-450
AST (U/l)	34	8-33
ALT (IU/l)	48	0-40
INR (second)	1.1	0.7-1.2
PT (second)	12.7	9-12
K+ (mmol/l)	4.9	3.5-5
Na (mmol/l)	141	135-145
Cr (Umol/l)	38.5	45-90
Urea (mmol/l)	2.4	3.5-7.5
CRP (mg/l)	0.57	0.5-1.0
Ph	7.3	7.35-7.45
pCO_2 (mmHg)	45	35-48
HCO_3 (mmol/l)	23	22-27
Lactate (Mmol/l)	2.5	0.5-1.6

Table 2. *Collective data summary of cyclopentolate adverse effects in children.*

Article, year of publication, Country	Patients	Amount of cyclopentolate administered	Time to seizure	Associated predisposing factors
Kennerdel and Wucher, 1972, USA [7]	11-month-old boy	One drop of 2% cyclopentolate hydrochloride in each eye	1 hour	Prematurity 36 weeks of gestation
	12-year-old boy		30 minutes	Known epilepsy
Büyükcam et al., 2012, Turkey [8]	3-month-old girl	One drop of 0.5% cyclopentolate hydrochloride and 2.5% phenylephrine hydrochloride in each eye on three occasions with a 10-minute interval	2 hours	Prematurity born at 28 weeks gestational age
Fitzgerald et al., 1990, Australia [3]	4.5-year-old boy	One drop of 1% cyclopentolate in each eye	70 minutes	Cerebral palsy
Hu et al., 2014, Canada [9]	Neonate born at 37 weeks and 3 days gestational age	One drop of Cyclomxydril (cyclopentolate 0.2% and phenylephrine 1%) to each eye	5 minutes	Congenital CMV infection without previous seizure
Demayo and Reidenberg, 2004, USA [1]	23-month-old boy	Cyclogyl (cyclopentolate hydrochloride) and 10% Neo-Synephrine (phenylephrine hydrochloride) eye drops	30 minutes	Previously healthy
Wygnanski-Jaffe et al., 2013, Israel [10]	5-year-old boy	One drop of cyclopentolate 1% installed twice in each eye with a 5-minute interval	Few minutes	Previously healthy
	6-year-old boy	One drop of cyclopentolate 1% in each eye with a 5-minute interval	10 minutes	Previously healthy
	3-month-old boy	Two drops of cyclopentolate 1% (5-minute interval between applications)	15 minutes	Previously healthy
	4-year-old boy	Cyclopentolate 1% drops were applied twice	Immediate	Previously health
	12-year-old girl	Cyclopentolate 0.5% eye drops twice with a 5-minute interval	30 minutes	Prematurity
Mwanza, 1999, Congo [11]	11-year-old female	Cyclopentolate 2%	45 minutes	NR

CMV, cytomegalovirus; NR, not reported.

occur after topical administration of cyclopentolate prior to the ophthalmoscopic examination, children with predisposing factors should be closely observed after the procedure [4]. There is no antidote for cyclopentolate toxicity; however, supportive care is often enough to manage toxic exposure [3,12,13]. Patients who remain asymptomatic for several hours are unlikely to develop long-term-related seizures or sequelae and may be discharged with a follow-up plan [6,13,14].

Conclusion

Cyclopentolate eye drops can increase the risk of seizure in the pediatric population. Children with central nervous immaturity are predisposed to an increased sensitivity to the systemic effects of cyclopentolate eye drops. As this case highlights, cyclopentolate instillation should be used with caution in children with neurological disorders.

Conflicts of interest
The authors declare that there is no conflict of interest regarding the publication of this article.

Funding
None.

Consent for publication
Due permission was obtained from the patient to publish the case report.

Ethical approval
Ethical approval is not required at our institution to publish an anonymous case report.

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