Myoclonic seizure due to cyclopentolate eye drop in a preterm infant

Ayşe Büyükcam[1], H. Tolga Çelik[2], Ayşe Korkmaz[2], Murat Yurdakök[2]

[2]Division of Neonatology, [1]Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey. E-mail: dr.aysebaktir@gmail.com

SUMMARY: Büyükcam A, Çelik HT, Korkmaz A, Yurdakök M. Myoclonic seizure due to cyclopentolate eye drop in a preterm infant. Turk J Pediatr 2012; 54: 419-420.

Cyclopentolate is widely used in ophthalmology for its intense mydriatic and cycloplegic activity. Systemic side effects have been described in both adults and children. Myoclonic seizure is a rare side effect of eye drops that are used in eye examinations. We report herein a case of convulsion in a three-month-old girl following cyclopentolate hydrochloride and phenylephrine hydrochloride eye drops, which were used in advance of ophthalmoscopy for examination of retinopathy of prematurity (ROP). Physicians should be aware of the uncommon systemic side effects of cyclopentolate, and drops should be used in appropriate dosages.

Key words: myoclonic seizure, cyclopentolate, eye drop, side effect.

Cyclopentolate is widely used in ophthalmology for its intense mydriatic and cycloplegic activity. Systemic side effects, especially in the central nervous system (CNS), have been described in both adults and children[1]. Cyclopentolate is a muscarinic receptor antagonist similar to atropine[2]. We present the case of a three-month-old girl who experienced a myoclonic seizure lasting over one hour after application of 0.5% cyclopentolate hydrochloride and 2.5% phenylephrine hydrochloride (1 drop every 10 minutes, 3 times). Her seizures began three hours after application of the last eye drop dose.

Case Report

A three-month-old girl born at 28 weeks gestational age was admitted for her screening examination for retinopathy of prematurity (ROP). One drop of 0.5% cyclopentolate hydrochloride and 2.5% phenylephrine hydrochloride was instilled into each eye on three occasions with a 10–minute interval, and ophthalmological examination was performed two hours later. After the examination, a myoclonic seizure occurred, lasting for 10 minutes. Phenytoin 20 mg/kg was applied as the initial dose and continued with a maintenance dose of 4.5 mg/kg/day divided into two doses. Serum electrolytes were as follows: sodium (Na): 146 mEq/L, potassium: 3.42 mEq/L, chloride: 103 mEq/L, calcium: 9.02 mg/dl, phosphorus: 2.98 mg/dl, and glucose: 87 mg/dl. Cranial ultrasonography revealed no acute pathological finding that could have caused the seizure. Following the seizure, an electroencephalography was carried out but revealed no epileptiform activity. Four days later, she again received cyclopentolate hydrochloride and phenylephrine hydrochloride eye drops before ophthalmoscopy for ROP and laser operation was done. Ketamine was also given for the operation. A myoclonic seizure lasting over one hour occurred following the operation. Serum electrolytes were as follows: Na: 142 mEq/L, potassium: 3.30 mEq/L, chloride: 103 mEq/L, calcium: 8.25 mg/dl, phosphorus: 4.08 mg/dl, and glucose: 112 mg/dl; plasma pseudocholinesterase activity was 7465 U/L (5320-12920). Midazolam (0.1 mg/kg as a loading dose and 0.05 mg/kg/hour as the maintenance dose) and phenytoin (10 mg/kg as a loading dose) were given but the seizure persisted. The midazolam dosage was increased to 2 mg/kg/hour. No additional seizures occurred for two days, and midazolam infusion was stopped. She was discharged without any sequelae.

Discussion

Cyclopentolate is a cycloplegic agent used commonly in pediatric practice for refraction testing. It is a synthetic anti-cholinergic agent

that produces mydriasis and cycloplegia[3]. It is a muscarinic receptor antagonist similar to atropine[2]. Systemic drug absorption from the ocular route is well known. Although there is some absorption from the conjunctival sac, the majority of systemic absorption of the instilled drug takes place in the nasal meatus[2].

Cyclopentolate shares certain rarely occurring side effects with atropine, which include the possibility of epileptic seizures[4]. Rarely, generalized seizures can occur, but CNS toxicity is rare[5]. The CNS toxicity is due to anti-cholinergic action causing stimulation of the medulla and cerebral centers[3]. In view of the smaller body mass in children, the chances of toxicity are higher[6]. Especially in preterm infants, the risk of toxicity and side effects may be greater because of low body mass and immaturity of the cardiovascular, nervous and digestive systems[7]. Females, fair children and children with Down syndrome are also more prone to toxicity[3].

Grand mal seizure after application of cyclopentolate and phenylephrine for ophthalmoscopy and low level of pseudocholinesterase activity were reported together previously[4], but in the present case, the level of pseudocholinesterase activity was normal.

The other systemic side effects include the atropine-like effects of 'dry as a bone' due to inhibition of sweat and salivary glands (one of the first effects) and 'red as a beet' because of vasodilatation to lose heat to overcome impaired sweat gland functioning. Rare allergic reactions include urticarial rash, headache, nausea, and wheeze. Severe anaphylactic reactions have also been reported[5].

In preterm infants, an increased incidence of feeding difficulties, including abdominal distension and increased gastric aspirate, may be observed on the day of mydriatic instillation[8]. In our case, only myoclonic seizure was observed. None of the other side effects of cyclopentolate was observed.

Early recognition of the signs and symptoms of systemic toxicity is essential. Treatment is essentially symptomatic, with physostigmine being reserved for serious toxicity[5,9]. Precautions for preventing the side effects of mydriatic agents are avoiding over-dosage, using diluted dosage especially for preterm infants, and punctual occlusion for 3-4 minutes following application. Patients and their parents should be warned about these possible side effects.

REFERENCES

1. Lahdes K, Huupponen R, Kaila T, et al. Plasma concentrations and ocular effects of cyclopentolate after ocular application of three formulations. Br J Clin Pharmacol 1993; 35: 479-483.
2. Lee YC, Simamora P, Pinsuwan S, et al. Review on the systemic delivery of insulin via the ocular route. Int J Pharm 2002; 233: 1-18.
3. Bhatia SS, Vidyashankar C, Sharma RK, et al. Systemic toxicity with cyclopentolate eye drops. Indian Pediatr 2000; 37: 329-331.
4. Demayo AP, Reidenberg MM. Grand mal seizure in a child 30 minutes after Cyclogyl (cyclopentolate hydrochloride) and 10% Neo-Synephrine (phenylephrine hydrochloride) eye drops were instilled. Pediatrics 2004; 113: e499-500.
5. Jones LW, Hodes DT. Possible allergic reactions to cyclopentolate hydrochloride: case reports with literature review of uses and adverse reactions. Ophthalmic Physiol Opt 1991; 11: 16-21.
6. Palmer EA. How safe are ocular drugs in pediatrics? Ophthalmology 1986; 93: 1038-1040.
7. Sarici SU, Yurdakok M, Unal S. Acute gastric dilatation complicating the use of mydriatics in a preterm newborn. Pediatr Radiol 2001; 31: 581-583.
8. Rengstorff RH, Doughty CB. Mydriatic and cycloplegic drugs: a review of ocular and systemic complications. Am J Optom Physiol Opt 1982; 59: 162-177.
9. Gray LG. Avoiding adverse effects of cycloplegics in infants and children. J Am Optom Assoc 1979; 50: 465-470.