Grand Mal Seizure in a Child 30 Minutes After Cyclogyl (Cyclopentolate Hydrochloride) and 10% Neo-Synephrine (Phenylephrine Hydrochloride) Eye Drops Were Instilled

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ABSTRACT. A grand mal seizure is an unexpected, rare adverse event in a child receiving eye drops to dilate the pupils for an eye examination. A case is reported of a convulsion in a 23-month-old boy after he received Cyclogyl (cyclopentolate) and Neo-Synephrine (phenylephrine) eye drops before ophthalmoscopy. His serum sodium was 125 mEq/L, and he had low plasma pseudocholinesterase activity. Children exposed to organophosphate insecticides and other pseudocholinesterase inhibitors may be at risk for cyclopentolate toxicity. *Pediatrics* 2004;113:e499–e500. URL: http://www.pediatrics.org/cgi/content/full/113/5/e499; *seizures, cyclopentolate, eye drops.*

Patients undergoing ophthalmoscopy in hospital for various reasons are given eye drops often for cycloplegia and mydriasis to facilitate examination of the retina. The agents commonly used are 10% phenylephrine eye drops to dilate the pupils and Cyclogyl (cyclopentolate) in the form of 0.5% or 1% eye drops to paralyze the iris (cycloplegia) temporarily. Cyclogyl is a muscarinic receptor antagonist similar to atropine. It shares certain rarely occurring side effects with atropine, which include the possibility of epileptic seizures. We present the case of a toddler without a prior history of seizures that had a grand mal seizure lasting 30 minutes after he got 1 drop in each eye, every 5 minutes, of 10% Neo-Synephrine and 1% Cyclogyl, for a total of 3 drops of each over a 15-minute period. His seizures began 45 minutes after he received the last dose of each eye drop.

CASE REPORT

A previously healthy 23-month-old white male infant came by ambulance to the hospital because of second and third degree scald burns involving both feet and ankles in stocking distribution. This injury was incurred by his being immersed at 6 PM in a tub of hot water. He was brought to a local emergency department by his mother 4⅔ hours after the accident (she said she had been told by phone to wait and see whether his feet became blistered and swollen before coming in). He was triaged, stabilized, and burn-dressed in the local emergency department and transferred by ambulance to this hospital for treatment in our burn center.

He arrived at our emergency department ~7¾ hours after the scalding. His temperature was 37.6°C, his pulse was 160 beats per minute, and his respirations were 32 per minute. He was crying, withdrawn, and in pain. He didn't talk. His weight was 11.88 kg (25th percentile), height was 93 cm (a little less than the 95th percentile), and head circumference was 49 cm (50th percentile). He showed a normal physical examination, except for a diaper rash, and a normal neurologic examination. There was no external evidence of head trauma or other trauma apart from the scald burns involving both feet and ankles in a stocking distribution. Some were of partial thickness, but most were full thickness.

The local emergency department had referred his case to the City of New York Child Protective Services before he was transferred.

In our emergency department he was given 1 mg of morphine sulfate subcutaneously at 2:10 AM and a diphtheria-tetanus pediatric immunization at 3:30 AM. Silver sulfadiazine was put on the burn, and a dry, sterile dressing was applied. He was admitted to the inpatient pediatric burn service at 4 AM.

Because his injury was consistent with child abuse, we sought other evidence of trauma, hence the ophthalmology referral for eye examination including retinoscopy to detect retinal hemorrhage as a reflection of possible intracranial injury. It was during this visit to the ophthalmology clinic that the 30-minute seizure occurred at 3 PM, the day after the scald.

At 3:10 PM, serum electrolytes drawn during the seizure revealed a low serum sodium (125 mEq/L), high potassium (5.8 mEq/L), low chloride (93 mEq/L), normal bicarbonate (23 mEq/L), normal urea nitrogen (13 mg/L), and creatinine (0.4 mg %). At 3:15 PM he was given 1.2 mg of diazepam (0.01 mg/kg per dose) slowly intravenously, and the seizures stopped. Repeat serum electrolytes drawn 45 minutes later (4:54 PM) were essentially unchanged. In this second sampling, we also found normal magnesium (1.7 mEg/L) and calcium (9.7 mEg/L) but slightly elevated glucose (122 mg/dL), probably because of the glucose in the intravenous fluids.

No additional seizures occurred. There were no retinal hemorrhages. A brain computed tomography scan was normal. An electroencephalogram was not done. The question of whether there was a link between the seizures and the use of the eye drops led to testing the patient's plasma for pseudocholinesterase by SmithKline Beecham laboratory (King of Prussia, PA). A normal dibucaine number of 84 was found, but the enzyme activity observed of 1753 IU was low (normal: 3200-6600). Total serum proteins were 5.9 g/dL, and albumin was 3.4.

Social work investigation revealed a household consisting of maternal grandmother, mother, and 2 siblings: an emotionally disturbed 6-year-old half-brother and a possibly normal 3-year-old half-sister. The 2 siblings were fathered by a man different than the father of the patient. The mother had a history of drug abuse. She subsequently admitted to intentionally scalding the patient and went to jail. The patient and his 2 half-siblings were placed together in a foster home. At discharge the patient could walk and seemed to have warmed up a little bit to his caregivers. He has the beginnings of speech and a more cheerful affect.

DISCUSSION

Cyclopentolate is well absorbed, both into the eye and systemically, when given topically on the eye.[1–4]

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This is because both the conjunctival and nasal mucus membranes are good drug-absorbing surfaces,[5,6] and eye drops pass readily through the nasolacrimal duct into the nose. Cases have been reported of seizures[7,8] and other forms of anticholinergic toxicity[9,10] after application of cyclopentolate eye drops.

Cyclopentolate is an ester that is structurally similar to many other drugs with ester bonds metabolized by plasma pseudocholinesterase. Pseudocholinesterase hydrolysis is the likely pathway of cyclopentolate metabolism. The low level of pseudocholinesterase activity in this patient's serum combined with the normal dibucaine number indicates that this patient has inhibited but genetically normal enzyme activity. Studies of agricultural workers exposed to organophosphate insecticides, common pseudocholinesterase inhibitors, found that only modest reductions in measured enzyme activity,[11,12] such as seen in this patient, were associated with symptoms of organophosphate poisoning.

The low serum sodium (125 mEq/L) was probably a predisposing factor for the seizures, likely precipitated by high levels of cyclopentolate due to failure of normal metabolism of the well-absorbed drug by low activity of plasma pseudocholinesterase. Because the serum albumin was normal in this patient, we think that the low enzyme activity was caused by enzyme inhibition. The common inhibitors are organophosphorus insecticides. Although we were not able to identity a source of an enzyme inhibitor for this patient, children exposed to organophosphate insecticides in their environments or with mutant pseudocholinesterase may be predisposed to cyclopentolate toxicity.

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