Neurotoxic Effects of Topical Cyclopentolate

Surg Cdr A Rajeev*, Surg Cmde G Gupta, NM⁺, Surg Cdr KM Adhikari[#], Surg Cdr AK Yadav^{**},
M Sathyamoorthy⁺⁺

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Introduction

Intraocular drugs are used in paediatric practice for diagnostic procedures as well as in the treatment of ocular conditions. Cyclopentolate is used in situations requiring mydriasis and cycloplegia. Systemic absorption of the drug can occur transconjunctivally or via nasolacrimal duct through highly vascular nasal mucosa [1]. Some amount of drug entering the nasolacrimal system may be swallowed and absorbed through stomach.

Adverse effects are seen in upto 10% of cases. These include tachycardia, central nervous system (CNS) effects like restlessness, hallucination, psychosis, hyperactivity, seizures, incoherent speech and ataxia [2,3]. We describe a case in which a child had acute CNS manifestation following instillation of cyclopentolate. Child completely recovered after eight hours.

Case Report

A six year old boy was seen at the ophthalmology outpatient department of our hospital with complaints of redness of left eye. He had sustained a blunt trauma on eye brow of the same eye a week back when he had a fall on to the edge of a table. Intraocular injury was suspected and in order to dilate the pupil one drop of cyclopentolate 1% was administered thrice to the child at five minutes intervals. Thirty minutes after the instillation of eye drops the child became restless. He started behaving abnormally and started screaming that a dog is chasing him. He had ataxia and he was showing jerky movements of limbs with frequent tightening of limbs. Child had a pulse rate of 110/minute and his blood pressure was 120/100 mm of Hg (more than 95th percentile for his age). He maintained arterial saturation of oxygen at 95% in room air. The child was administered midazolam 0.3 mg/kg to calm him down for an urgent computed tomography (CT) scan of brain (to rule out head injury in view of abnormal behavior with recent a history of trauma on

left eye brow). CT scan brain was essentially normal. Investigations like complete blood count, blood sugar, liver function tests (LFT), blood urea, serum creatinine and electrolytes were normal. Cerebrospinal fluid (CSF) examination was carried out to rule out CNS infection as acute viral meningoencephalitis can manifest with behavioral abnormalities in children. The CSF was essentially normal. Child was given supportive treatment with intravenous fluids with constant cardiac and respiratory monitoring. Child recovered completely over next eight hours.

Discussion

Cyclopentolate is a synthetic anticholinergic agent which produces mydriasis and cycloplegia. The advantages of this drug are rapid onset of action and recovery. Side effects are uncommon. Systemic toxicity is dose related. Toxicity includes inappropriate behaviour, visual and auditory hallucinations and cerebellar signs. CNS effects are due to stimulation of medulla and cerebral centers by the anticholinergic action of cyclopentolate. Infants, young children and children with neurological impairment are more susceptible to systemic side effects [3,4]. A case of acute progressive midbrain haemorrhage after intraocular cyclopentolate in an adult has been described [5]. Cardiovascular side effects of the drug include tachycardia and hypertension. Systemic side effects are also reported with intraocular administration of drugs like beta blockers and pilocarpine. Treatment is primarily supportive. Patient should be protected from self-inflicted injury by physical or pharmacological restraint. Diazepam or midazolam can be used for the purpose. The specific antidote is physostigmine, which can be used in severely agitated patients who are not responding to other therapies. Child with respiratory failure may require mechanical ventilation. In our case child had acute CNS manifestations in the form of restlessness, hallucinations and ataxia following intraocular instillation of

*#Classified Specialist (Paediatrics), INHS, Asvini, Mumbai-05. *Commanding Officer, **Classified Specialist (Paediatrics), ++Resident (Paediatrics), INHS Sanjivani, Cochin.

cyclopentolate. He responded to supportive treatment and recovered completely.

Topical ophthalmic preparations are widely prescribed by ophthalmologists. Steps that can be taken to reduce systemic absorption and toxicity include using the lowest available concentration of the drug, not exceeding recommended number of drops (instill one drop of 0.5% or 1% in eye followed by one drop of 0.5% or 1% after five minutes, if necessary), occluding the lacrimal passage after topical administration, blotting away excess drops after administration and using micro drops (drops with volume of 5.6 microlitres as against volume of 35.4 microlitres of a standard drop). In neonates and infants cyclopentolate and phenylephrine combination is preferred due to lower cyclopentolate concentration and reduced risk for systemic reaction [6].

In conclusion, greater care is required while administering intraocular drugs to children. Present case highlights important side effects of a topically administered drug. Physicians should be aware of all adverse effects of drugs which they are prescribing routinely so that optimum treatment can be given without delay and without subjecting the patients to unnecessary

investigations. The medical and paramedical staff should use the drug in the prescribed dose and methods to minimize systemic absorption should be instituted.

Conflicts of Interest

None identified

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Journal Scan

Pacchiarotti I, Mazzarini L, Colom F, Sanchez Moreno J, Giradi P, Kotzalidis GD. Treatment resistance Bipolar Depression: towards a new definition. *Acta Psychiatr Scand* 2009; 120: 429-40.

Though the most distinctive feature of a bipolar disorder is mania/ hypomania, depression is clearly the most recurrent, predominant and burdensome. Bipolar depression accounts for the largest part of the morbidity and appears primarily responsible for the reduced quality of life. Large evidence shows that bipolar depression is clinically and therapeutically different from unipolar depression however the concept of treatment resistance remains similar to that of unipolar depression. Author reviewed the evidenced based therapeutic options with structured searches through the indexed randomised controlled trials (RCTs) and open label trials and subsequently summarized the conceptual and operational definition of treatment resistant depression. Various previous researches attempted to include failure of lithium or combination of mood stabilizers and antidepressants for the concept of treatment resistant bipolar depression. Lithium has been found more effective in mania than bipolar depression. Food and Drug Administration (FDA) has not approved any anticonvulsant or antidepressants for bipolar depression. Fixed dose olanzapine-fluoxetine combination or quetiapine monotherapy is presently the only approved modality.

Author proposed that firstly new remission criteria be developed with the help of available scales as residual mood symptoms in bipolar depression is associated with higher risk of relapse and poor functional outcomes. While planning treatment operational criteria should distinguish bipolar I and II depression as the latter have a well recognized depressive prominent polarity. Different degrees of severity within bipolar depression were proposed in a stepwise manner based on the failure to respond to a definite treatment algorithm over eight week duration contingent to the improvement on Clinical Global Impression (CGI) and Hamilton depression (HAM-D) score. Higher dosage of quetiapine was recommended for bipolar I depression for better mood stabilization to avoid mixed state, which entails higher risk of suicide. Low dosage of the fluoxetine was also advised in the combination for the same reason. Author introduced the concept of intractable and involutional bipolar depression if the depression failed to respond to first three or all four steps respectively. This proposed criteria in the light of existing literature definitely merits consideration for inclusion in our clinical practice.

Contributed by

Col PS Bhat*

*Associate Professor (Dept of Psychiatry), AFMC, Pune-40.