ACUTE PSYCHOSIS INDUCED BY TOPICAL CYCLOPENTOLATE EYE DROPS IN A YOUNG CHILD

Nagesh HN*1, Suresh VC.2, Suresha KR1, Jensy Reshma D'souza3, Lavanya A2, Khadse PA2

1Department of Pharmacology, Akash Institute of Medical Sciences and Research Centre, Devanahalli, Bengaluru.
2Department of Psychiatry, Akash Institute of Medical Sciences and Research Centre, Devanahalli, Bengaluru.
3Department of Ophthalmology, Akash Institute of Medical Sciences and Research Centre Devanahalli, Bengaluru.

ABSTRACT

Central anticholinergic syndrome (CAS) is a clinical entity which shows central and peripheral effects produced by over dosage or abnormal reaction to clinical dosage of anticholinergic drugs. Anxiety, delirium, disorientation, hallucinations, seizures, tachycardia, hyperpyrexia, mydriasis, vasodilatation, gastric and urinary retention can be observed during CAS. Cyclopentolate is an anticholinergic drug, used in cycloplegic eye examinations for mydriasis. A 9 year old male child complaining of itching and redness in both eyes since 6 months visited to ophthalmology department. To examine eye proper single drop of Cyclopentolate eye drops was instilled to both eyes 3-4 times at an interval of 10 min. After 1 hour the child became restlessness, irritable and started talking irrelevantly. General and neurological examination did not reveal any abnormality. Psychiatrist’s opinion revealed normal consciousness and orientation, muttering to self, delusion of persecution, visual hallucination and impaired judgment was noted. Based on the above findings, a rare adverse effect of drug-induced psychosis was suspected. The child was given single dose of Midazolam 2 mg IV in ICU to reduce behavioral abnormality and the child’s behavior reverted to normal within 8 hours.
KEYWORDS: central anticholinergic syndrome, cyclopentolate eye drops, psychosis.

INTRODUCTION
Central anticholinergic syndrome (CAS) was first described by Longo in 1966. The estimated frequency of this syndrome varies between 1 and 11.2%. CAS results from the inhibition of muscarinic cholinergic neurotransmission and manifested by central nervous system (CNS) effects or peripheral nervous system effects, or both. These include tachycardia and CNS effects like restlessness, hallucination, psychosis, hyperactivity, seizures, incoherent speech, and ataxia. In addition to anticholinergics, drug classes that have anticholinergic properties include antihistamines, antipsychotics, antispasmodics, cyclic antidepressants, and mydriatics causes CAS.

CASE REPORT
A 9 year old male child weighing 24 kg came to ophthalmology outpatient department with complaints of itching and redness in both eyes since 6 months. For the purpose of examination of eye proper single drop of Cyclopentolate 1% eye drops was instilled to both eyes 3-4 times at an interval of 10-15 minutes. After 1 hour the child became restlessness, irritable and started talking irre relevantly. On examination child’s vitals were stable. General and neurological examination did not reveal any abnormality. Psychiatrist’s opinion revealed normal consciousness and orientation, muttering to self, delusion of persecution, visual hallucination and impaired judgment was noted. All the possible causes for abrupt onset of symptoms were ruled out and drug-induced psychosis was suspected. The child was admitted to intensive care unit (ICU) for observation. To reduce behavioral abnormality child was given single dose of Midazolam 2 mg IV infusion at the rate of 0.05-0.4/mg/kg/h and the child’s behavior reverted to normal within 8 hours and the child was discharged without any sequel. ADR causality assessment was assessed using Naranjo’s probability scale and was found to be probable.

DISCUSSION
Acetylcholine (ACh) and its receptors are widely distributed in the brain. ACh is important in regulating many functions including the sleep-wake cycle, memory, alertness, orientation, and analgesia. An absolute or relative reduction in cholinergic activity in the central nervous system (CNS) can result in anticholinergic syndrome, which can manifest with a variety of signs and symptoms. Dryness of the skin and mouth, dermal flushing, fever, irritability, abdominal distention, urinary retention, feeding intolerance, psychosis, ataxia, hallucinations,
convulsion, coma, tachycardia with normal blood pressure, arrhythmia, and death can be observed after multiple instillations of the eye drops or accidental ingestion by infants, children and patients with neurologic disorders (particularly Down syndrome).\[^{4}\]

Topical ophthalmic preparations are widely prescribed by ophthalmologists, which may cause serious ocular or systemic adverse effects. Systemic absorption of these drugs occurs primarily via nasal mucosa and conjunctiva, nasolacrimal duct, oropharynx, digestive system, and skin.\[^{2,5}\] Children, particularly infants, are more prone to systemic adverse effects of topical eye drops because of their lower body mass and blood volume, immature metabolism, and immaturity of excretory, nervous, and cardiovascular systems.\[^{6}\] The toxicity is dose-related.\[^{7}\]

Cyclopentolate is an anticholinergic, antimuscarinic tertiary amine with atropine-like actions whose topical administration to eyes causes mydriasis and cycloplegia. It has gained widespread use as the cycloplegic drug of first choice for most children over the age of 1 year and allows many optometrists and ophthalmologists to carry out quick successful cycloplegic refractions with few complications.\[^{5}\]

When instilled topically in the eye, it is well absorbed into the eye. In our case, cyclopentolate eye drops could be absorbed by capillary and reached the brain via angulus venosus of deep cerebral veins and cavernous sinuses. 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 5 min, if necessary), occluding the lacrimal passage after topical administration, blotting away excess drops after administration. The precise epidemiologic profile of the occurrence of cognitive and/or behavior changes in patients treated with anticholinergic agents remains unknown, especially due to inherent biases and confounding factors in each population studied, including treatment regimens, age group, underlying pathology, and so on.\[^{8}\]

Some cases have been reported of agitation, visual hallucinations and other forms of anticholinergic toxicity after application of cyclopentolate eye drops.\[^{3,9}\] Adverse systemic effects of cyclopentolate that have been well documented, include tachycardia, generalized urticaria and seizures. Acute psychosis has also been reported after topical instillation, and it occurs more frequently in children with little weight.\[^{3}\]
In our case acute psychosis was developed due to systemic adsorption of cyclopentolate and it could be dose dependent. Children with low body mass were more prone to develop toxicity. They normally occur within 20-30 minutes of administration and subside within 4-6 hours with no permanent sequel and the patients having no recollection of the hallucinations. Another possible reason for the hallucinations could be the similarity of cyclopentolate's amino-dimethyl group to the amino-methyl group found in LSD (a hallucinogenic agent).\cite{7,10} CNS toxicity is rare, though some studies have reported an incidence of psychosis as high as 4\%.\cite{3}

Present case demonstrated that a rare CNS toxicity (acute Psychosis) is possible in younger children when cyclopentolate eye drop are administed. Early recognition of signs and symptoms of systemic toxicity is very important in the management of illness. Most of the signs and symptoms can resolve spontaneously.

One should be aware of all adverse effects of the drugs which they are prescribing routinely so that optimum treatment can be given. The medical and paramedical healthcare staff should use the drug in the prescribed dose and methods to minimize systemic absorption.

REFERENCES


9. 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.