



Respiratory depression after accidental nasal ingestion of brimonidine eye drops in infant



Ali Gunes^{a,*}, Hasan Balik^a, Servet Yel^a, Halil Kocamaz^b, Mehmet Bosnak^c

^a Dicle University Medical School, Department of Pediatrics, Diyarbakir, Turkey

^b Pamukkale University Medical School, Department of Pediatrics, Denizli, Turkey

^c Gaziantep University, Medical School Department of Pediatric Critical Care, Gaziantep, Turkey

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ABSTRACT

Objectives: Brimonidine tartrate is an alpha-2 agonist used for glaucoma treatment. It can lead to serious poisoning symptoms when misused by children.

Case report: In this case report, 3 months-old male patient with severe central nervous system depression and respiratory arrest as a result of accidentally nasal instillation of 1 cc brimonidine tartrate that benefited from mechanic ventilation and naloxone treatment was presented.

Conclusion: This case report suggested, that misuse of nasal brimonidine eye drop could result in serious respiratory distress and central nervous system depression. Mechanical ventilation and naloxone administration can be useful for these patients.

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1. Introduction

Brimonidine tartrate (Alphagan; Allergan Inc., Irvine, Calif) is an α -2 adrenergic agonist that used for glaucoma treatment.¹ Although this medicine rarely lead to poisoning, serious systemic side effects have been observed in children following overdose or improper use.² Serious intoxication cases of brimonidine poisonings resulting from oral administration have been reported before,³ but we could not find a case with poisoning symptoms due to nasal administration of brimonidine in a literature search. Previous studies have reported that giving naloxone as an antidote is not useful in cases with severe poisoning.^{4,5} In this study, a three months-old male case with brimonidine intoxication was presented. Saline was administered in nasal orifice of the patient at first, because the problem was supposed to be a nasal congestion resulting from influenza infection that lasting for three days. However, respiratory failure developed and mechanical support

ventilation has to be started and the clinical symptoms resolved with three times of 0.015 mg/kg intravenous naloxone.

2. Case presentation

A three month-old male child with sighs and shallow breathing admitted to our hospital. Patient history revealed that approximately 1 cc brimonidine tartrate content eye drop had been instilled accidentally to his nares by his grandmother to relieve nasal congestion confusing the dropper with physiological saline 2 h ago. Physical condition of the patient was poor and there were hypotonia, hypothermia, perioral cyanosis on his physical examination. His Glasgow coma scale was five, his pupils were miotic and unresponsive to light. Pupillary light reflexes were also absent. His heart rate was 157/min, with shallow breathing rate of 10/min. Oxygen saturation was 85% on room air. Respiratory sounds were barely evaluated due to hypoventilation and arterial blood pressure was normal. Patient also had bladder globe. The other physical examination results were normal. Complete blood count and biochemical parameters were normal. Sinus tachycardia appeared in the electrocardiography. Chest X-ray was normal. Nasal oxygen and intravenous fluids were given in emergency room then the patient instantly transferred to the pediatric intensive care unit. Patient was intubated due to severe respiratory failure and low oxygen saturation. He was connected to a mechanical ventilator.

* Corresponding author. Tel.: +90 412 248 5782; fax: +90 412 248 84 40.

E-mail addresses: draligunes@gmail.com (A. Gunes), drhasanbalik12@hotmail.com (H. Balik), dr.servetyel@hotmail.com (S. Yel), halilkocamaz@yahoo.com (H. Kocamaz), mbosnak@hotmail.com (M. Bosnak).

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Naloxone was given intravenously as antidote at the dose of 0.015 mg/kg every 3 min consecutively 3 times until his findings get improve. After control of breathing and heart rate the patient was extubated with normal neurological findings compatible with his age at the end of the hospital admission day. Then, the patient was discharged with complete recovery without any sequel on the fourth day of admission.

3. Discussion

Brimonidine is an α -2 selective adrenergic agonist used to treat open-angle glaucoma or ocular hypertension and it lowers intra-ocular pressure by reducing aqueous humor liquid production or by increasing elimination through uveoscleral outflow.⁴ When excessively instilled in the eye of children, it is carried to nasal through nasolacrimal duct and can lead to systemic side effects by absorbing from the nasal mucosa.⁶ Primary metabolism of brimonidine is in the liver. After taken orally, it is metabolized in liver and its metabolites are excreted from kidney.⁴ Drugs for nasal administration directly get into systemic circulation by surviving from elimination in liver and can cause less dose and more serious side effects.² In addition, because of child's blood brain barrier (BBB) is not completely matured and brimonidine is highly lipophilic, it can lead to severe central nervous system depression when transmitted to central nervous system.^{2,7} These findings can lead to fatigue, weakness, lethargy, apnea, bradycardia, hypotension, respiratory depression and coma, especially in children.² In the majority of the case reports presented in previous studies, the following findings were determined in patients; weakness, lethargy, apnea, respiratory distress and recovery with symptomatic treatment.¹ However, our patient had respiratory depression, hypotension and coma. His oxygen saturation was low. In literature, bradycardia and respiratory depression have rarely been reported.⁴

We postulated that the reason, why our patient went into coma and his respiratory suppressed to require mechanical ventilation, may be due to late admission to hospital and/or nasal admission of brimonidine. In most of the studies, patients usually have admitted to the hospital in the first hour and signs of toxicity generally occurred as a result of oral administration. In our study, the patient admitted to hospital 2 h late. Children completely recover from brimonidine intoxication in hours through symptomatic treatment.

Naloxone can be helpful for patients with hypotension unresponsive to adequate fluid therapy and for severe cases.⁸ Nevertheless, some reports show that naloxone is useless for respiratory depression, coma and central nervous system depression in brimonidine intoxication.^{4,5} In our study, intravenous naloxone was given following mechanical ventilation and the patient was discharged with full recovery.

In conclusion, brimonidine misused in children can cause serious side-effects. Thus, it is important to explain the details of side effects in children to while prescribing this drug for treatment of cataract in adults. Severity of side effects increases with nasal use. Symptomatic treatment can be sufficient in mild cases, however naloxone will be beneficial for patients with central nervous system depression.

Conflicts of interest

None declared.

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References

1. Rangan C, Everson G, Cantrell FL. Central alpha-2 adrenergic eye drops: case series of 3 pediatric systemic poisonings. *Pediatr Emerg Care*. 2008;24:167–169.
2. Levy Y, Zadok D. Systemic side effects of ophthalmic drops. *Clin Pediatr (Phila)*. 2004;43:99–101.
3. Soto-Perez-de-Celis E, Skvirsky DO, Cisneros BG. Unintentional ingestion of brimonidine antiglaucoma drops: a case report and review of the literature. *Pediatr Emerg Care*. 2007;23:657–658.
4. Dauber GP. Is brimonidine ophthalmic a safe therapy for infants? *J Clin Pharm Ther*. 2006;31:289–292.
5. Mungan NK, Wilson TW, Nischal KK, et al. Hypotension and bradycardia in infants after the use of topical brimonidine and beta-blockers. *J AAPOS*. 2003;7:69–70.
6. Shell JW. Pharmacokinetics of topically applied ophthalmic drugs. *Surv Ophthalmol*. 1982;26:207–218.
7. Palmer EA. How safe are ocular drugs in pediatrics? *Ophthalmology*. 1986;93:1038–1040.
8. Hoffmann U, Kuno S, Franke G, et al. Adrenoceptor agonist poisoning after accidental oral ingestion of brimonidine eye drops. *Pediatr Crit Care Med*. 2004;5:282–285.