



Cardiorespiratory depression in infant following unintentional ingestion of brimonidine tartrate, and use of naloxone as an antidote: Case report

Abdulmajeed Mohammed Alrashoud¹, Abdullah Mohammed Kamel¹, Mohammed Yahya Tairi¹, Imran Ahmad Gattoo², Seham Abdu Alhajoori³

¹ Pediatric Emergency Consultant, Department of Pediatric Emergency, King Saud Medical City, Riyadh, KSA, Saudi Arabia

² Pediatric Emergency Specialist, Department of Pediatric Emergency, King Fahad Medical City, Riyadh, KSA, Saudi Arabia

³ Pediatric Nursing Specialist, King Saud University, Riyadh, KSA, Saudi Arabia

Abstract

Context: Brimonidine, a topical ophthalmic medication used to treat open-angle glaucoma or ocular hypertension. Brimonidine misused in children can cause serious side effects. Oral ingestion of brimonidine eye drops can lead to cardiorespiratory and central nervous system depression.

Objective: We report an 80-days-old boy who developed cardiorespiratory depression due to accidental ingestion of brimonidine, and he responded to antidote Naloxone.

Patient: The patient is an 80-days-old boy who came to the PED as a case of drug ingestion (brimonidine tartrate) that was used as eye drops by his older brother for his open-angle glaucoma. His four-year-old sister accidentally put the drops in his mouth. After 1 hour, the mother noticed that the baby started to cry, refused to feed, and became irritable. On arrival to our emergency at evening time, the patient was agitated, irritable, unable to open his eyes, drooling, and started to develop bradycardia and bradypnea.

Conclusions and Outcome: Oral ingestion of brimonidine eye drops can lead to cardiorespiratory and central nervous system depression. Naloxone can be a beneficial modality of treatment to reverse these symptoms in such patients. Early presentation and prompt use of antidote in such cases can even eliminate the need for mechanical ventilation.

Keywords: brimonidine, naloxone, cardiorespiratory depression

Introduction

Brimonidine tartrate is a selective central α_2 adrenergic agonist agent chemically similar to clonidine and another ocular α_2 agonist, apraclonidine. Brimonidine suppresses aqueous humor production and increases uveoscleral outflow. It is used as eye drops to treat glaucoma and ocular hypertension and as an intraocular pressure-lowering agent [1]. Although this medicine rarely leads to poisoning, systemic severe side effects have been observed in children following overdose or improper use [2]. In case of toxicity due to intraoral intake of ocular drops, brimonidine can gain rapid access to the central nervous system (CNS) and lead to cardiorespiratory depression requiring fast supportive management in the intensive care unit. Although it has a good safety profile, some adverse effects have been reported after ocular administration. However, there is not much information regarding oral ingestion of brimonidine in the pediatric population [2]. Previous researches have reported that giving Naloxone as an antidote is not helpful in cases with severe poisoning [3]. In this study, 80 days old boy with accidental ingestion of brimonidine tartrate was presented to our Pediatric Emergency Department (PED) in cardiorespiratory depression. The infant was successfully managed with Naloxone as an antidote, which otherwise, as per the current literature, has a doubtful role in reversing cardiorespiratory depression caused by brimonidine.

Case report

A previously healthy, Eighty-day-old boy presented to our

PED, King Saud Medical City (KSMC), Riyadh, KSA) as a case of drug ingestion (brimonidine tartrate) that was used as eye drops by his older brother for his open-angle glaucoma. His four-year-old sister accidentally put the drops in his mouth. After 1 hour, the mother noticed that the baby started to cry, refused to feed, and became irritable, so she brought the baby to our PED.

On arrival to our emergency at evening time, the patient was agitated, irritable, unable to open his eyes, drooling, but vitally stable HR:120 b/m, RR: 25/min, BP: 90/50 mmHg Spo2: 98% RA, Temperature: 36.9 C. Pupils was constricted 2 mm and sluggish reaction to light, GCS: 13/15. The rest of the systemic examination was normal.

The patient was connected to the monitor, and suction was done and evaluated correctly. One and a half hours later patient started to develop bradycardia and bradypnea; vital signs were: HR: 80 b/m RR: 8 b/m, BP: 90/45 mmHg Spo2: 100% on 15 L/m by nonrebreather mask. Pupils were constricted 1-2 mm sluggish reacting to light.

We ordered Naloxone by a dose of 0.05mg/kg as an antidote; the Naloxone was given and prepared for possible intubation. After 15 minutes patient started to improve, and the pupils were 2-3 mm sluggish reacted to light, HR: 130 b/min, RR: 28 bpm, Pediatric Intensive Care Unit (PICU) was consulted. Thirty minutes later patient again became bradycardic, and bradypnea so we gave the second dose of Naloxone with the same dose. After 10 minutes patient started to improve.

The patient was observed and monitored in our PED for 3

hours with typical vital signs: HR: 110 b/m RR: 22 b/m Spo2: 100% by a nonrebreather mask, GCS: 14/15, pupils 2-3 mm reacted to light, and he did not need Naloxone more, so patient shifted to PICU. During PICU admission patient was stable with no further respiratory compromise; the patient did not need further naloxone doses nor need of mechanical ventilation. The patient was discharged to home with an excellent clinical condition.

Discussion

Brimonidine, a topical ophthalmic medication used to treat open-angle glaucoma or ocular hypertension, is a highly selective and potent α -2-adrenoceptor agonist that reduces intraocular pressure by diminishing aqueous humor production and increasing its elimination through the uveoscleral pathway. Brimonidine can enter the systemic circulation via the ocular structures, and it has an elimination half-life of 2 to 5 hours^[3]. Signs and symptoms of intoxication were similar in adults and children. Because the blood-brain barrier in children is not that mature, drugs like brimonidine can easily cross from systemic circulation to the brain and lead to various kinds of side effects, including bradycardia, hypotension, respiratory depression, lethargy, and sleepiness. The children were tired, lethargic, apneic, and unable to be aroused^[4]. Severe intoxication cases of brimonidine resulting from accidental ingestion of ocular drops have been reported worldwide^[4], but none of such a case has been reported from Saudi Arabia. Also, previous studies did not support the use and effectiveness of Naloxone as an antidote in severe poisoning^[3]. There is no approved antidote for the treatment of brimonidine toxicity. Pediatric studies have described the use of activated charcoal after accidental oral ingestion of brimonidine eye drops and intravenous Naloxone in established brimonidine toxicity. Still, no consistent benefit has been observed^[5]. Naloxone can benefit patients with hypotension unresponsive to adequate fluid therapy and severe cases. Nevertheless, some reports show that Naloxone is useless for respiratory depression, coma, and central nervous system depression in brimonidine intoxication^[4].

Our case report is an 80-days-old boy who developed cardiorespiratory depression due to accidental ingestion of brimonidine, and he responded to antidote Naloxone.

In literature, patients have been reported to present varied symptoms. Still, cardiorespiratory depression as a presenting feature has been rarely reported; notably, such a case has never been reported in the kingdom of Saudi Arabia before. Also, in literature, the role of Naloxone for reversing the cardiorespiratory depression has not been established as some studies favor its role, and others found it not that significant in reversing the cardiorespiratory depression due to brimonidine^[5]. We gave Naloxone on a trial basis to our patient, who showed a dramatic response in reversing cardiorespiratory depression and didn't need mechanical ventilation. The patient was discharged with complete recovery. The effectiveness of Naloxone in our patients and not need for mechanical ventilation may be attributed to early presentation and prompt use of Naloxone in our case.

Conclusion

In conclusion, unintentional ingestion of medications is one of the leading causes of poisoning in children. Brimonidine misused in children can cause serious side effects. Thus, it is

essential to explain the details of the side effects in children while prescribing this drug for treatment. Oral ingestion of brimonidine eye drops can lead to cardiorespiratory and central nervous system depression. The use of naloxone can be a beneficial modality of treatment to reverse these symptoms in such patients. Early presentation and prompt use of antidote in such cases can even eliminate the need for mechanical ventilation.

Abbreviations

CNS: Central Nervous System

KSMC: King Saud Medical City

PED: Pediatric Emergency Department

PICU: Pediatric Intensive Care Unit

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None

Conflict of interest

None declared

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