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Topiramate Associated Hypohidrosis and Hyperthermia

FARUK INCECIK
M OZLEM HERGÜNER
SAKIR ALTUNBASAK

ABSTRACT

Topiramate is a new antiepileptic drug, used for treatment of partial onset seizure and refractory seizures. Although it is well tolerated in children, some adverse effects including hypohidrosis and hyperthermia are reported. We present two children with epilepsy who were treated with topiramate and developed hypohidrosis and hyperthermia.

Key words: *Adverse event, Epilepsy, Hyperthermia, Hypohidrosis, Topiramate.*

INTRODUCTION

Topiramate is a new antiepileptic drug, effectively used for partial onset seizures, infantile spasms, and refractory absence(1). Chemically it is a sulfamate-substituted monosaccharide and structurally resembles carbonic anhydrase inhibitors with a weak inhibitory effect in vitro. Topiramate has different mechanisms of action: (*i*) blockade of voltage-dependent sodium channel in the neuronal membrane, (*ii*) blockade of kainate type of glutamate receptor, (*iii*) enhanced γ aminobutyric

From Cukurova University Medical Faculty, Department of Pediatric Neurology, Adana, Turkey.

Correspondence to: Faruk Incecik, Toros mah. Bariş Manço Bulv. Gökçenbay-2 sitesi, B blok, kat: 8, no: 16, Adana, Turkey. E-mail: fincecik@yahoo.com

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acid (GABA) activity at GABA receptors, and (*iv*) inhibition of carbonic anhydrase isoenzyme(2).

Topiramate is an effective drug, safe and tolerated well in children. Most common adverse effects are central nervous system related, such as somnolence, confusion, concentration difficulties, and behavioral change. Anorexia, weight loss, nephro-lithiasis, hypohidrosis, and acute glaucoma are also reported(3-5). We report hypohidrosis in two children who were administered topiramate.

CASE REPORT

***Case* 1:** A five year-old girl was admitted to our clinic with complex partial epilepsy secondary to intracranial hemorrhage. In the past, she was treated with several antiepileptic drugs (AEDs). Because of poor seizure control, the medication was changed to oxcarbazepine and one month later to topiramate. Topiramate was started with initial dose of 1 mg/kg/day, and increased weekly up to 7 mg/kg/day. Topiramate was initially well tolerated, and the patient became seizure-free. Four months after reaching the target dose, she developed intermittent hyperthermia, which disappeared after bathing and cooling. Moreover, her mother noticed the loss of sweat despite high ambient temperature. There were no clinical or laboratory indicators of infection. Sweat test was performed with pilocarpine iontophoresis, however sweat could not be collected. Topiramate was stopped, and the sweat test was repeated after one month. The sweat chloride concentration was 60 mEq/L. Hyperthermia also disappeared after discontinuation of topiramate.

***Case* 2:** A 7-year-old boy was admitted with symptomatic partial epilepsy secondary to phenylketonuria. He was medicated with oxcarbazepine. Because of poor seizure control on oxcarbazepine, topiramate was added in a dose of 1 mg/kg/day, and gradually increased to 6 mg/kg/day. Topiramate was well tolerated, and the child became seizure-free. Six months later, he developed daily hyperthermia, and felt tired after normal exercise. He also reported loss of sweating despite a high ambient temperature. Hyperthermia disappeared, and sweating became normal, after discontinuation of topiramate.

DISCUSSION

Physiologic sweating is a complex function regulated by the sympathetic system as well as factors and neurotransmitters localized in the periglandular nerves or within human sweat glands(6). In addition, isoenzymes of carbonic anhydrase I and II have been identified in human eccrine sweat glands(7). Although the mechanism of the hyperthermia and hypohidrosis associated with topiramate is not well known, it is speculated that the inhibition of carbonic anhydrase and sweat dysfunction may be responsible for this side effect(2). Topiramate might affect electrolyte channels or transporters in sweat glands as well as in neurons; however it is not clear whether the sodium channels in sweat glands are structurally similar to the neuronal channels. Topiramate also has an inhibitory effect on some carbonic anhydrase isoenzymes (II and IV)(2).

We conclude that topiramate may cause fever and decreased sweating, however these effects are reversible. Children treated with topiramate should be warned regarding these potential adverse effects, to facilitate early withdrawal of drug and symptomatic relief.

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Chikungunya Infection in Neonates

GOURI RAO PASSI
YASMIN ZAKARYA KHAN*
DS CHITNIS†

ABSTRACT

We describe two neonates in whom chikungunya infection was confirmed by RNA PCR. Important clinical features include apnea, fever, erythematous maculopapular rash and generalized hyperpigmentation.

Key words: *Chikungunya, Newborn.*

INTRODUCTION

An epidemic of chikungunya fever was raging in many states of India in the second half of year 2006. There are not many reports of clinical features of confirmed chikungunya infection in newborns. We report 2 cases with chikungunya, confirmed by RNA PCR, with their distinct clinical picture and briefly review literature available on neonatal chikungunya infection.

*From the Department of Pediatrics and †Microbiology, Choithram Hospital & Research Center, Indore; Madhya Pradesh, *Department of Pediatrics, Subishi Hospital, Khargone, Madhya Pradesh, India.*

Correspondence to: Gouri Rao Passi, 139, Indrapuri, Indore, Madhya Pradesh, India.
E-mail: gouripassi@hotmail.com

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CASE REPORT

***Case* 1:** A single term 3 Kg male baby was born to a second gravida mother by cesarian section. The mother had pregnancy induced hypertension and was on antihypertensives from the 2nd trimester. One day prior to delivery the mother developed high fever with severe joint pains. In view of the chikungunya epidemic in Khargone (a town in the state of Madhya Pradesh in India where the baby was born), a clinical diagnosis of chikungunya was made and she was treated conservatively with antipyretics. The baby cried immediately after birth and was on breast feeds from day 1. On day 3 the baby stopped feeding and developed fever of 39ºC. He also developed generalized maculopapular rashes. Twelve hours later he developed 2 episodes of apnea with cynosis and was referred to our hospital for further management.

At admission child was excessively irritable and crying constantly. He had a generalized maculopapular rash but heart rate, respiratory rate and blood pressure were normal for age. He had no organomegaly and cardiovascular examination was normal. Sepsis screen, blood culture was taken and empirical antibiotics were started. He did not have any recurrence of fever or apnea in hospital and the rash slowly disappeared over 3 days. The child was discharged on exclusive breast feeds after 7 days. His investigations were as follows: Hb 13.5 g/dL, total leukocyte count 11,200/mm^3, platelet count 2.2×10^9/L and CRP was negative. Blood culture was normal and PCR for chikungunya RNA was positive.

***Case* 2:** A 21-day-old male baby presented to us with intermittent fever from 5 days of age. He was born to