The Efficacy of Topiramate in Benign Paroxysmal Torticollis of Infancy: Report of Four Cases

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Dr Yaghini conceived the main idea of the study, provided patient information, conducted patient follow-up, and revised and approved the final manuscript as submitted; and Ms Badihian and Dr Badihian prepared the final manuscript, contributed to gathering of patient data, and approved the final manuscript as submitted.

DOI: 10.1542/peds.2015-0868

Accepted for publication Dec 21, 2015

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FINANCIAL DISCLOSURE: The authors have indicated they have no financial relationships relevant to this article to disclose.

FUNDING: No external funding.

POTENTIAL CONFLICT OF INTEREST: The authors have indicated they have no potential conflicts of interest to disclose.

abstract

Benign paroxysmal torticollis (BPT) is a rare paroxysmal dyskinesia and 1 of the childhood periodic syndromes presenting with recurrent stereotypic episodes of torticollis, usually accompanied with some of the nonheadache features of migraine such as vomiting and ataxia. Although the nature of BPT may seem benign, its recurrent episodes can mimic attacks of epilepsy and expose the infant to unnecessary hospitalization and adverse effects of inappropriate medications. There is no approved medication for the disease, but a few studies have suggested that cyproheptadine is useful. However, use of this agent has not been confirmed as effective for these patients, and the safe dosage for children aged <2 years has not yet been established. We report 4 patients who exhibited a successful response to treatment with topiramate (their episodes of BPT stopped). Considering the underlying relation of BPT with migraine, the satisfactory response of our patients to topiramate, and the safety of this medication in neonates and children, topiramate seems to be an effective and safe medication for the reduction and elimination of BPT episodes. In addition, 1 of our case subjects (patient 4) confirmed this finding by exhibiting an explicit dependence in the regularity and duration of her attacks with topiramate. Topiramate seems to be an effective medication for the prophylaxis of BPT episodes. Further studies and clinical trials are recommended.

Benign paroxysmal torticollis (BPT) is a rare paroxysmal dyskinesia that was first described by Snyder in 1969.1–3 It is a childhood periodic syndrome categorized in the main document of the International Classification of Headache Disorders, Third Edition.4 BPT presents with recurrent stereotypic episodes of paroxysm of torticollis during infancy.5 The episodes occur spontaneously, are self-limited, and often have a specific regularity.5, 7 BPT is more prevalent in girls (~70%), and most episodes occur in the morning.1, 8 These episodes usually begin between age 2 and 8 months, improve by age 2 years, and disappear by age 3 to 4 years.1, 5, 9 As the child grows up, the attacks disappear, but they may be replaced by a modified form, including attacks of ataxia, benign paroxysmal vertigo of childhood, and, later in childhood, by migraine, other childhood periodic syndromes, or motion sickness disease.1, 6, 7, 10, 11

Some of the nonheadache features of migraine such as vomiting, ataxia, pallor, irritability, malaise, apathy, drowsiness, photophobia, tears, nystagmus, and agitation may be associated with or rapidly follow the BPT attacks.1, 4, 6–8, 12, 13 The presence of structural, genetic, and metabolic disorders should therefore be ruled
out to support the diagnosis of BPT. A family history of similar childhood syndrome, migraine, or motion sickness on the father’s or mother’s side is common.

Although >40 years have been passed since the initial description of BPT, there is no known treatment of the disease, and no clinical trials have been conducted. The nature of BPT seems to be benign; however, BPT episodes are distressful for the infant and are usually associated with symptoms such as vomiting and agitation, which can lead to frequent hospitalizations. Because BPT is almost certainly underrecognized by pediatric practitioners, they may order extensive and unnecessary testing for the patient. All of these scenarios inflict an unnecessary psychological and financial burden on the patient’s family. A safe treatment is therefore essential for managing the disease.

Some authors have suggested that cyproheptadine may help prevent BPT attacks, but the safe dosage for patients aged <2 years has not been established, and torticollis attacks usually begin in infancy. Accordingly, safe medication is still lacking for these patients. Topiramate can be used in neonates and children aged <2 years for various therapeutic purposes such as migraine (and its variants) and convulsion. Because of the probable association between BPT and migraine, it may be an appropriate treatment for BPT. Here we report 4 new case subjects with BPT in whom treatment with topiramate was successful.

**CASE REPORTS**

Patient information is summarized in Table 1.

**Patient 1**

A 22-months-old girl had attacks of torticollis associated with agitation that had started at 3 months of age. During her first attack, which lasted for 2 hours, the patient was admitted to the emergency department, where acetaminophen was prescribed for her agitation; she was discharged after the attack. After the recurrence of another attack 2 weeks later, the patient was prescribed phenobarbital in the hospital, and she was diagnosed with a seizure disorder; her attacks were not controlled, however, and she experienced her third episode of torticollis and agitation in 2 weeks. She was then referred to our pediatric neurology clinic (at ~5 months of age). Neurologic examination, EEG, and brain computed tomography (CT) scan results were all normal. Due to the pattern and duration of the attacks, the fact the patient was conscious during the attacks, and because of the clinical and paraclinical findings, BPT was considered a more likely diagnosis, and topiramate was initiated at a dosage of 2 mg/kg daily. The patient experienced no other episodes of torticollis except a 10-minute attack at 18 months of age. Her developmental process is normal although she started walking at 18 months of age. She experienced no adverse effects of topiramate. She has a 15-year-old brother who has migraine without aura.

**Patient 2**

A 28-months-old boy had experienced initial attacks at 8 months of age of head tilting associated with vomiting that lasted 8 hours. He was admitted to the hospital; no medication was prescribed, and he was discharged after observation. The patient returned to the hospital in 3 weeks with another episode of torticollis associated with vomiting. His second attack lasted for 4 hours and remitted spontaneously. The patient was then referred to our pediatric neurology clinic (at ~9 months of age). Results of the neurologic examination, growth and development:

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Gender</th>
<th>Age at First Episode, mo</th>
<th>Duration of Episode, h</th>
<th>Accompanying Symptoms</th>
<th>Initial Diagnosis</th>
<th>Neurologic Examination, EEG, Brain CT Scan</th>
<th>Previous Medication</th>
<th>Family History of Migraine</th>
<th>Current Age, mo</th>
<th>Development</th>
<th>Topiramate Dosage, mg/kg daily</th>
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<tr>
<td>1</td>
<td>F</td>
<td>3</td>
<td>2</td>
<td>Agitation</td>
<td>Seizure disorder</td>
<td>Normal, Normal</td>
<td>Phenobarbital</td>
<td>Brother</td>
<td>22</td>
<td>Walking with help at age of 18 mo</td>
<td>2</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>8</td>
<td>8</td>
<td>Vomiting</td>
<td>Suspicion of drug toxicity</td>
<td>Normal, Normal</td>
<td>None</td>
<td>Mother</td>
<td>28</td>
<td>Normal</td>
<td>2</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>6</td>
<td>2–3</td>
<td>Vomiting</td>
<td>Seizure disorder</td>
<td>Normal, Normal</td>
<td>Phenobarbital, phenytoin, clonazepam</td>
<td>Mother &amp; Father</td>
<td>28</td>
<td>Normal</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>3</td>
<td>2</td>
<td>None</td>
<td>Seizure disorder</td>
<td>Normal, Normal</td>
<td>Phenobarbital</td>
<td>Father</td>
<td>22</td>
<td>Walking at age of 18 mo</td>
<td>4</td>
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CT, computed tomography; F, female; M, male.
assessments, EEG, and brain CT scan were all normal. Normal clinical and paraclinical findings, the pattern and duration of the attacks, and the fact the patient was conscious during the attacks indicated a likely diagnosis of BPT. Topiramate was started at a dosage of 2 mg/kg daily in 2 separate doses. He experienced no other episode of torticollis. Although his parents stopped giving the child his medications after he was 1.5 years old, no more attacks have occurred since now. He experienced no adverse effects with topiramate. The patient's mother reports a history of migraine without aura.

**Patient 3**

A 28-months-old girl presented with episodes of torticollis associated with vomiting and agitation from the age of 6 months. Her first attack lasted ~1 hour, and phenobarbital was prescribed. A diagnosis of seizure disorder was made in the emergency department. After the first attack, several attacks occurred and led to her admission to the hospital. Each attack lasted for 2 to 3 hours, although no medication was prescribed; after remission of the episode, the patient was discharged. Considering the recurrence of the attacks, she was referred to our pediatric neurology clinic at 8 months of age. The neurologic examination, EEG, and brain CT scan revealed no abnormal findings. After all evaluations, based on the pattern and duration of the attacks, the fact the patient was conscious during the attacks, and the clinical and paraclinical findings, we considered BPT to be the more likely diagnosis. The patient was started on topiramate at a dosage of 2 mg/kg daily, and the phenobarbital was tapered. The patient experienced no additional attacks and no adverse effects of topiramate. Her mother reports migraine without aura.

**Patient 4**

A 22 months of age female child, started having attacks of torticollis associated with crying at the age of 3 months for the first time. Her attacks occurred every month, and each attack lasted for 2 hours. After experiencing recurrent attacks, the patient was seen repeatedly in pediatric clinics; she was treated, unsuccessfully, with phenobarbital, phenytoin, and clonazepam as antiepileptic medications. The patient was referred to our pediatric neurology clinic at 6 months of age. She had a normal neurologic examination, EEG, and brain CT scans. Considering the normal findings, the pattern and duration of the attacks, and the fact the patient was conscious during the attacks, we proposed BPT as a more probable diagnosis. She was therefore started on topiramate at a dosage of 2 mg/kg daily, which shortened the duration of her episodes to 10 minutes and made them less frequent (1 episode every 2 months). The patient stopped having attacks after age 1 year. At the request of her parents, the patient's dosage of topiramate was tapered but, during the tapering, she experienced another attack, which lasted for 3 hours. Topiramate was therefore restarted at the previous dosage. Because the dosage of 2 mg/kg was not beneficial this time, the dosage was increased to 4 mg/kg, and the episodes stopped. Although the patient’s developmental process is normal, she needs help walking at age 22 months. She experienced no adverse effects of topiramate. Her father reports a history of migraine without aura.

**DISCUSSION**

In this study, we describe 4 case subjects with BPT who exhibited a satisfactory response to topiramate. This medication can be used in neonates as an anticonvulsant, as an adjunctive therapy and monotherapy for epilepsy, and as migraine prophylaxis for children aged >2 years.19,20 Our findings suggest that topiramate is beneficial in the treatment of BPT.

BPT presents with recurrent stereotypic episodes of paroxysm of torticollis during infancy.5 Episodes disappear spontaneously, usually within a few hours or days; however, they may last up to 7 days or for only few minutes in some patients.1,7 Various symptoms can occur during the episodes or rapidly afterward. Longitudinal studies have shown that children with BPT can later develop benign paroxysmal vertigo (with accompanying ataxia), which may next be followed by development of cyclic vomiting (so-called “abdominal migraine”) and, finally, by more classic migraine.9,21 These children frequently have a history of motion sickness, particularly when riding in automobiles.1,6,10 The pathogenesis of BPT is unknown, but some underlying phenomena have been suggested.1 In some cases, a correlation with genes associated with familial hemiplegic migraine such as CACNA1A and PRRT2 has been reported.5,7,22 A family history of a similar childhood syndrome, migraine, and motion sickness on the father’s or mother’s side is common as well.6–9,15,16

The fact that BPT has a benign nature and is self-limited should not make treatment or management unnecessary. Not only are these attacks disabling, patients also experience frequent unnecessary hospitalizations because of BPT-associated symptoms. They may be misdiagnosed and unnecessarily exposed to the adverse effects of inappropriate medications and intravenous therapy such as antiepileptic drugs. The psychological and financial burden on the family for admission of these patients to the hospital should not be overlooked. Although it has been suggested that cyproheptadine can prevent attacks
and be beneficial in painful episodes, no specific study or clinical trial is available for evaluation of its efficacy in BPT. In addition, the safe dosage of cyproheptadine has not yet been established in children aged <2 years, which is noteworthy because episodes of BPT start in infancy. No symptomatic treatment, including meclizine, dimenhydrinate, and chlorpromazine, has been shown to be beneficial. Therefore, no definitive and safe treatment for this disease exists.

A common family history of migraine in patients with BPT, correlation with genes such as CACNA1A and PRRT2, accompaniment of some nonheadache features of migraine with BPT episodes, and the replacement of this disorder with migraine in later childhood in some patients all suggest BPT is a variant of migraine. This possibility prompted us to consider that a migraine medication might be beneficial in patients with BPT. Therefore, the lead author (as a pediatric neurologist) administered topiramate, a safe antimigraine drug that can also be used in infants aged <2 years, for these cases. All case subjects exhibited a considerable response to treatment, and none experienced any of the adverse effects of topiramate, including cardiovascular, central nervous system, dermatologic, or gastrointestinal symptoms. Episodes of torticollis were controlled after administration of topiramate in 3 cases. Case four experienced recurrent episodes with tapering of the drug, which were again controlled by increasing the dosage of topiramate. These findings support the therapeutic effect of this medication in the management of BPT and decrease the probability of accidental improvements in BPT episodes in our cases. Cases 1, 3, and 4 were formerly unsuccessfully treated with phenobarbital, which indicates BPT does not have a seizure disorder nature. Previous suggestions regarding managing BPT with cyproheptadine also confirms it as a migraine variant.

CONCLUSIONS

Our findings suggest that topiramate may be a safe and effective medication for the treatment of BPT in infants and children. However, considering the few number of cases, the low frequency of episodes, and the variable duration of the episodes and intervals between individual paroxysms, further studies on more patients with longer follow-up periods are needed to support this finding and investigate the therapeutic effect of topiramate in patients with BPT.

ABBREVIATIONS

CT: computed tomography
BPT: benign paroxysmal torticollis

REFERENCES


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*Pediatrics* originally published online March 8, 2016;

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