

# Tourette Disorder Treated With Valproic Acid

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**Abstract:** Valproic acid was successfully prescribed for a 10-year old boy suffering from Tourette's Disorder with a co-morbid bipolar diagnosis. Valproic acid has demonstrated efficacy in reducing the total number of motor tics, their frequency, intensity, complexity, and impairment in a patient who had failed to respond to numerous other medications. Valproic acid may be a useful agent to consider for children with treatment-resistant Tourette's disorder.

**Key Words:** Tourette's Disorder, Tic disorder, Bipolar disorder, Attention deficit hyperactive disorder, Valproic acid

(*Clin Neuropharm* 2014;37: 00–00)

Tourette's Disorder is a childhood-onset neuropsychiatric condition characterized by multiple motor and vocal tics. The estimated prevalence of a lifetime diagnosis of Tourette's syndrome is 3.0 per 1,000.<sup>1</sup> The common co-morbidities include obsessive compulsive or attention deficit/hyperactivity disorders (ADHD), anxiety, and depression. Haloperidol and pimozide are approved medications for treating patients with Tourette's Disorder. Drugs of antipsychotic, antidepressant, alpha-adrenergic, or anticonvulsant properties, and benzodiazepines have been prescribed with variable outcomes. Valproic acid has been prescribed to suppress abnormal movements in Huntington's Disease<sup>2</sup> and Sydenham Chorea.<sup>3</sup> Valproic acid successfully ameliorated severe complex motor tics in a child with a treatment-resistant Tourette's Disorder.

## CASE STUDY

A 10 year old white male was hospitalized due to worsening and persistently abnormal movements for two weeks. Presenting with body twitching and contortion, his arms were quickly flexing and extending. He displayed rapid head bobbing, eye blinking, squinting, tongue protrusions, and shoulder shrugging. The patient experienced compulsive, irresistible movements, of touching, jumping, crawling, and rolling on the floor. The motor tics affected head, neck, trunk, and limbs. Soft phonic tics included throat clearing and sniffing. The constant hyperkinetic movements were severe, resulting in sweating, tachypnea, and physical exhaustion. He recently lost 10 pounds since the motor tics had worsened.

Tics manifested at age of five years old, in a waxing and waning course. They were exacerbated during stress, anxiety,

excitement, or anger and diminished during sleep. The patient had a history of bipolar, anxiety, and attention-deficit hyperactivity disorders. The family history revealed tic, mood, ADHD, and anxiety diagnoses.

Brain magnetic resonance imaging without contrast and computerized axial tomography of the head did not reveal intracranial abnormalities. Electroencephalography was interpreted as an unremarkable wake, drowsy, and sleep recording. Normal laboratory results included the chemistry panel, complete blood count, thyroid-stimulating hormone, thyroid hormones (free T4 and free T3), copper, ceruloplasmin, magnesium, anti-streptolysin O, rheumatoid factor, antinuclear antibody, anti-neutrophil cytoplasmic antibody, and somatomedin C.

A neurological examination was conducted. Cranial nerves II through XII were intact. Muscle tone and strength were normal. The patient exhibited multiple tics including facial grimacing, head bobbing, and a symmetrical hand tremor. Deep tendon reflexes were symmetrically 2+ out of 4. There was no ankle clonus and plantar responses were flexor. Sensory examination was intact to touch and proprioception. Finger tapping was slow and sequential movement were clumsy for age. He was able to sit, stand, and get up from the sitting to the standing position. Walking, balance on either foot, and forward tandem gait were unremarkable.

The patient had been receiving daily medication including lithium, risperidone, and fluoxetine. On admission, lithium and risperidone were discontinued to clarify diagnosis and rule out medication-induced tics. Co-administration of oxcarbazepine and guanfacine resulted in significantly fewer tics; however, they returned three weeks after hospital discharge. Over the next year, aripiprazole, clonazepam, lorazepam, and levetiracetam were prescribed without efficacy. Clonidine caused sedation. Atomoxetine induced hallucinations. Worsened irritability was observed with quetiapine. Lithium was resumed and yielded a decrease in irritability, but the motor tics did not improve, even when combined with aripiprazole and fluoxetine. The bouts of motor tics continued once or twice per month, lasting one or two weeks each time. The vocal tics reminded mild and nearly a daily occurrence.

Valproic acid was introduced at 250 mg daily and resulted in a blood level of 23 ug/ml. The rapid body twitching, jumping, and other complex movements subsided within one week. The Yale Global Tic Severity Scale (YGTSS) score dropped from 80 to 24, the Yale Motor Tic Severity score declined from 24 to 9, and a vocal tic severity score decreased from 6 to 5. Improvement included a reduced total motor tic number, frequency, intensity, complexity, and degree of impairment. The tic-free intervals sustained for a few days, sometimes for a few weeks. Mild facial grimacing and eye blinking is observed briefly. The vocal tics reminded mild and unchanged. Valproic acid had been continued for 2.5 years until he left the treatment setting. Tics no longer grossly impaired his function or daily activities. Improvement had been maintained for over two years and his quality of life was significantly better.

## DISCUSSION

Valproic acid quickly diminished complex motor tics in a child who had failed to respond to numerous other medications.

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Conflicts of Interest and Source of Funding: The authors have no conflicts of interest to declare.

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Consent: Written informed consent was obtained from the patient about publication of this report. A copy is available on request.

Author contributions: The authors were the only persons preparing this manuscript.

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DOI: 10.1097/WNF.0000000000000013

The symptom reduction had been achieved across all dimensions of motor tic severity on YGTSS. Valproic acid may be a useful agent to consider in treating Tourette's Disorder with severe complex movements. Topiramate has been reported to be effective in treating motor tics.<sup>4</sup> In this case, a comorbid bipolar disorder might indicate valproic acid to have been a reasonable choice due to its antimanic effects. Since pharmaceutical options to maintain sustained tic reduction are limited, in chronic or unresponsive cases, valproic acid should be considered; however, the adverse effects of blood and liver dyscrasias do not suggest its use as a first-line treatment.

Given the fluctuating course of tics and because many patients can suppress them voluntarily for a period of time, the effectiveness of oxcarbazepine and guanfacine might have been a placebo phenomenon. The structured environment and increased attention by hospital staff could have contributed to a transient remission. Clonidine and guanfacine had failed in this case, but might be more helpful in individuals with milder tics. Their favorable tolerability is clinically desirable.<sup>5</sup>

The etiology of Tourette's Disorder is unknown. It has postulated to have a genetic contribution with dopamine and gaba-amino butyric acid (GABA) system dysfunction.<sup>6</sup> Those abnormalities are also observed in chorea that may share some biological underpinnings with Tourette's Disorder.<sup>7</sup> Valproic acid, a GABA enhancing agent, has been prescribed to suppress abnormal movements in Huntington's Disease and Sydenham Chorea.

It could have a therapeutic value in the treatment of refractory Tourette's Disorder, as noted in this case.

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