

# Valproate for the Treatment of Resistant Tourette Syndrome With Comorbid Trichotillomania: a Case Report

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**Keywords:** Tourette syndrome; Trichotillomania; Valproate

## Case Report

Tourette syndrome (TS) is characterized by multiple motor and one or more vocal tics for more than 1 year with no 3-months tic-free interludes prior to age of 18 (or 21 in some classificatory systems) with a male preponderance, fluctuating course, and polygenetic transmission with variable penetrance [1]. Common comorbidities include ADHD, OCD and low impulse control [2]. Only when disabling or socially embarrassing that tic treatment is indicated. FDA-approved treatments include antipsychotics haloperidol (Serenace<sup>®</sup>) and pimozide (Orap<sup>®</sup>). Extrapolation into the use of atypical antipsychotics, notably, risperidone (Risperidal<sup>®</sup>) is currently considered the state of the art. Alfa-2 adrenergic agonists, exemplified by clonidine (Catapres<sup>®</sup>), are also effective especially with comorbid ADHD [3]. Medications used for refractory cases are legion [4,5] (Table 1). Trichotillomania is an impulse dyscontrol disorder; now classified within OCD spectrum [6]. TS with comorbid trichotillomania is ubiquitous given the underlying neurocircuitry in common. Both represent frontal-striatal dysfunction [7].

Here we are reporting a difficult-to-treat case of TS with comorbid trichotillomania that failed sequential trials of haloperidol, pimozide, risperidone, aripiprazole (Abilify<sup>®</sup>) and clonidine. Clomipramine (Anafranil<sup>®</sup>) was tried for trichotillomania, as well as sertraline (Zoloft<sup>®</sup>), but to no avail. When shifted to valproate (Dtepakine<sup>®</sup>) monotherapy, response was very impressive for both; TS and trichotillomania. This might open new venues for treatment of such complicated clinical scenarios.

A 14-year-old Syrian youngster was referred to us from dermatologic clinic, in accompaniment of his parents for assessment of distressing hair-pulling resulting in disfiguring alopecia areata. He is the product of an uneventful NVD of a monogamous non-consanguineous marriage, unremarkable developmental trajectories, youngest of 3 sibs and a high achiever student. Family history is notable for OCD father and a parental aunt with anorexia nervosa. He was diagnosed with TS at age of 11 by a neurologist for multiple motor (blinking, shoulder shrugging, sniffing) and phonic (throat clearance) tics. He was prescribed antipsychotics (haloperidol, pimozide, risperidone, aripiprazole) in succession but the response was mediocre at best in addition to a number of adverse drug reactions he developed on these medications (hyperprolactinaemia and tremors on haloperidol and risperidone, akathisia on aripiprazole and sinus tachycardia on pimozide). In Syria, he was seen by a psychiatrist who prescribed a combination of multiple-dose clonidine

• Antipsychotics (haloperidol, pimozide, risperidone, ziprasidone, amisulpride...)
• DA depleters (tetrabenazine)
• α 2 agonists (clonidine, guanfacine)
• BDZ (clonazepam)
• Anticonvulsants (topiramate)
• Dopaminomimetics (ropinirole)

**Table 1:** Pharmacologic Options in TS.

• VGS/KC blockade
• GABA potentiator
• Signal transduction downstreaming
• DA blockade
• Histone deacetylase inhibition

**Table 2:** Mechanisms of Action of Valproate.

and clomipramine. The kid could not tolerate sedative effect of this 'combo' and parents stopped it shortly. He was shifted to sertraline, uptitrated to 200 mg/d, mostly for trichotillomania but in vain. Baseline laboratory investigations, including TFTs, UTox screen, ASO titre and EEG, were unrevealing. OCS and bipolarity were meticulously ruled out. We opined to embark on a trial with valproate. Pre-treatment Y-GTSS (Yale-Global Tic Severity Scale) and MGH (Massachusetts General Hospital) hair-pulling scale were contemplated and read 65 and 22 respectively. Valproate was uptitrated to 1200 mg/d over 2 weeks. For the first time, the youngster felt less distressed, tics began to be less frequent and less severe and most importantly, was shown to be less engaging in bouts of trichotillomania. Habit Reversal Therapy (HRT) sessions were then introduced alongside medications. At W-4, 6, 8 and 12, he kept exponentially improving in terms of tics and hair-pulling. This was well reported by parents too, who noticed brightening of mood and better overall self-esteem. At W-20, Y-GTSS and MGH hair-pulling scales were readministered and read 30 and 9 respectively. Valproate was well-tolerated. LFTs, CBC with platelet count and *S. valproate* were checked periodically and were within laboratory reference ranges. Serum valproate was therapeutic and maintained at 100 µg/ml. Multiple drug trials, psychometry and parents' reports would strongly militate against placebo response in this case.

Valproate is a pluripotent psychotropic drug with a composite mechanism of action (Table 2). We assume allosteric enhancement of GABA<sub>A</sub> inhibition and dopaminergic blockade, inter alia, by valproate might explain its utility in TS and trichotillomania. This goes in tandem with a case report of trichotillomania that responded favourably to valproate. A recent systematic review and meta-analysis of 5 RCTs of valproate use in TS was conducted, only one RCT was positive and another showed superiority to haloperidol. We suggest that valproate remain a viable option in such complicated cases [8-11].

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**Received** April 11, 2015; **Accepted** April 27, 2015; **Published** May 04, 2015

**Citation:** Naguy A, Al-Tajali A (2015) Valproate for the Treatment of Resistant Tourette Syndrome With Comorbid Trichotillomania: a Case Report. J Psychiatry 18: 286 doi: [10.4172/2378-5756.1000286](https://doi.org/10.4172/2378-5756.1000286)

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