Editöre Mektup / *Letter to Editor*

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To the Editor,

Tourette syndrome (TS) is characterized by chronic motor and vocal tics. Treatment of TS is usually challenging, thus most of the drugs used for TS may be insufficient. We will present a 12 year-old boy successfully treated by Aripiprazole, an off-label drug for TS.

S, 12 year old boy, was referred to our outpatient unit due to his multiple motor and vocal tics. Motor tics were characterized by eye blinking, eye gazing, squinting, head and arm jerks, leg jerks, copropraxia. His vocal tics included whistling, echolalia, palilalia, grunting and coprolalia. He was diagnosed with TS according to DSM-IV criteria (1). Additionally, there was no history of birth complications, delayed development or streptococcal infections but a positive family history of TS in his brother. Besides, his biochemical tests, ceruloplasmin level, EEG, and cranial MRI had no abnormalities.

He has been treated by a number of drugs since the age of 6; atypical neuroleptics (Risperidone up to 2mg/day for 2 years, Quetiapine 25-100mg/day for 2 months, Ziprasidone 40mg/day for 3 months), typical neuroleptics (Haloperidol 5-10mg/day for 1 year, Pimozide 2-8mg/day for 2 years), SSRIs (Fluoxetine up to 20 mg/day for 2 years, Citalopram up to 40mg/day for 1 year, Sertraline up to 50mg/day for 6 months), mood stabilizers (Carbamazepine 200mg/day for 6 months, Valproic acid 500mg/day for 8 months) and the others (Bornaprin 4mg/day for 1 year). But all these treatments resulted in no sufficient improvement in his tics.

Hence we decided to try Aripiprazole, a new antipsychotic drug. We began Aripiprazole 10 mg/day initially. We increased the dosage to 20 mg/day when a partial improvement was observed ten days later. After Aripiprazole 20 mg/day for about 3 weeks, the severity of tics decreased dramatically. Only eye blinking tic, which exacerbated during stress, slightly persisted. YGTSS (Yale Global Tic Severity Scale) total score was 99 at the beginning and dropped to 27 at the end of the first month. Furthermore no important side effects were observed. Only mild somnolence was observed during the first week.

The basal ganglia and related thalamocortical circuitry have been implicated in the underlying pathophysiology of TS. There are a number of drugs effecting to these systems. These drugs work by D2 antagonism, GABAergic effects, or unknown mechanism. However, these drugs do not improve tic symptoms in some patients with TS. Recently some drugs have been used in drug resistant tic disorder because of their different working mechanism.

Aripiprazole is a stabilizer of the dopamine/serotonin system. Its suggested mechanism is the partial agonism on D2 receptors, as it binds more to D2 G-protein bound receptors than to those which are not D2 G-protein bound (2). The affinity of the drug for D2 is 4-to 20 times lower than that of haloperidol, chlorpromazine, or other typical antipsychotics (3). Only aripiprazole has this special feature as a dopamine system stabilizer. Besides, it shows a partial agonist activity on 5HT1A receptors and

antagonism on 5HT2A receptors. Most neocortex 5HT1A receptors are situated in glutamatergic pyramidal neurons. These receptors have an inhibitory action, which would reduce the excitatory glutamatergic output. It is believed that part of the control of tics would stem from this control in the glutamatergic projection pathways. These different effect mechanisms can be superior to other drugs in treating persistent tic symptoms.

Our drug resistant case might have responded to Aripiprazole more likely because of the mechanisms mentioned above. There are also similar findings in a number of case series (Bubl et al 2006 (4), Davies et al 2006 (5), Miranda et al 2007 (6), and Stenstrom et al 2008 (7)). We think that Aripiprazole may have more positive efficacies in the treatment of TS. So the treatment with Aripiprazole should be considered in children and adolescents with TS especially in treatment resistant cases.

Kaynaklar:

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