

Letter to the Editor

Tardive Dystonia and the Use of Cannabis

A 48-year-old man diagnosed with paranoid schizophrenia presented to our department complaining of neck discomfort and involuntary movements in the orofacial region. He reported that his first complaint was difficulty in his relationship with his wife when he was 28 years old and then hearing voices was added. Since his complaints increased into the next 2 years he was taken into a psychiatric hospital and diagnosed with paranoid schizophrenia. He had used one 200-mg zuclopenthixol depot injection per month, and biperiden 6 mg and sulpride 100 mg daily for 1 year. At the end of the 8-month treatment with these drugs, he presented with involuntary movements of the orofacial region, with difficulty swallowing and chewing. At the same time, he developed involuntary sustained contraction of the neck muscles. These involuntary movements exacerbated over the next months until his speech became dysarthric and his neck became severely disabled. Five months after the initiation of his symptoms he began smoking cannabis 3 or 4 times a week for 2 years and observed that his involuntary movements significantly decreased. For this reason, he continued smoking cannabis to self-treat his symptoms until he was arrested due to smuggling. He stopped smoking cannabis and his symptoms then exacerbated and became fixed during the 7 months he was in prison. The administration of the same antipsychotic drugs was continued in prison.

On admission to our clinic the general physical examination was normal. Neurological examination showed an alert patient with dysarthric speech. His head was turned to the left and upwards due to the sustained contraction of his neck muscles. There were continuous oro-bucco-linguo-masticatory dyskinesias as well. The neurological examination was normal, except for fixed dystonic posturing in the neck muscles and orofacial dyskinesia. Family history of movement disorders and psychiatric

disease was negative. Cranial and cervical magnetic resonance imaging, electroencephalogram, full blood count, serum chemistry, thyroid tests, serum ceruloplasmin level, and 24-h urinary copper excretion were all normal. Genetic testing for Huntington's disease was negative. Acanthocytes were not observed in the peripheral blood smear. The patient's Extrapyramidal Symptom Rating Scale (ESRS) score was 31 (1).

Psychiatric examination revealed blunted affect, anxious mood, coherent speech, and mildly increased talkativeness. His hygiene was poor and he had sporadic loosening of associations. Anorexia and insomnia were described. The patient reported that he had auditory hallucinations, delusions of persecution, reference, and grandeur, and thought withdrawal, and reported he was capable of thought broadcasting. The patient and his family reported that he had experienced auditory and visual hallucinations, bizarre delusions, and delusions of persecution, reference, and grandeur since he was 28 years old. He had not had any manic episodes. He was diagnosed with schizophrenia, as he was unable to perform his job or engage in social activities, and because his psychotic symptoms, such as hallucinations and delusions, were constant since he stopped smoking cannabis. Subsequently, the patient was diagnosed with antipsychotic-induced tardive oro-bucco-linguo-masticatory dyskinesia and tardive neck dystonia. At that time, olanzapine was started (up to 20 mg d⁻¹) over a period of 4 weeks, during which time his orofacial dyskinesia began to gradually abate. Two months after the initiation of olanzapine the patient continued to experience remarkable improvement in his orofacial dyskinesia and his psychiatric symptoms were controlled, but tardive dystonia in his neck remained unchanged. Subsequently, diazepam (10 mg d⁻¹ PO) for 1 month did not improve the patient's tardive dystonia, nor did the addition of baclofen (up to 30 mg d⁻¹) for 2 months decreased his dystonic symptoms. Consequently, botulinum toxin was injected into the bilateral trapezius and splenius capitis muscles, but the symptoms of tardive dystonia did not diminish. As botulinum toxin therapy failed to provide long-lasting

improvement of his dystonic symptoms, sormodren (up to 8 mg d⁻¹) was administered. At the start of the 6th month of our follow-up (with respect to olanzapine start date), the patient had a trial of treatments sequentially by about monthly intervals (sormodren, 8 mg d⁻¹; gabapentin, 1200 mg d⁻¹), but again there was no clinical change in his tardive dystonia, although he was free of orofacial dyskinesia while on olanzapine.

The mechanisms of tardive dyskinesia and dystonia remain poorly understood; numerous theories have been proposed, including dopamine receptor supersensitivity, catecholamine hyperactivity, and lack of g-aminobutyric acid (GABA). Presynaptic dopamine receptor blockage in the substantia nigra and ventral tegmentum by serotonergic neurons, secondary oxidative stress, and neuron death are among the other hypotheses (Yetimalar et al., 2007).

The endocannabinoid system plays a role in the control of movement. As numerous cannabinoid CB1 and CB2, and vanilloid VR1 receptors are located in the areas that are key to movement, such as the basal ganglia and cerebellum, adds support to this hypothesis. Some studies have reported that plant-derived synthetic and endogenous cannabinoid agonists have powerful actions, mostly inhibitory effects on motor activity in humans and laboratory animals (Richter, 1994; Müller-Vahl, 1999; Fernández-Ruiz, 2005). In addition, changes in CB1 receptors in different neurodegenerative diseases were observed in postmortem studies, and symptoms were reduced in Parkinson's disease, Huntington's disease, and Tourette's syndrome after the administration of cannabinoids. Anecdotal reports have suggested that cannabis might alleviate symptoms in a variety of neurological conditions, including dystonia. High levels of cannabinoid receptor bindings are found presynaptically in the globus pallidus and substantia nigra pars reticulata. It has been proposed that cannabinoid receptor stimulation enhances GABA transmission and reduces overactivity of the globus pallidus, thereby reducing dystonic symptoms (Fox, 2002; Sagredo, 2007). An open trial that included 5 patients with dystonia due to a variety of causes reported that symptoms improved with oral synthetic cannabinoid receptor agonist use (Consroe et al., 1986).

Tardive dystonia in our patient did not improve following several drug regimens. Our patient's involuntary movements decreased significantly while he smoked cannabis for 2 years. Although we did not have the opportunity to administer and observe the effects of an oral cannabinoid agonist while treating this patient, as cannabinoid agonists are not available in Turkey, we think that cannabinoid agonists might be an appropriate choice in the treatment of intractable tardive dystonia.

In summary, we report a patient that developed tardive dystonia secondary to antipsychotic use that was not successfully treated with several therapy regimens; however the patient remained free of the symptoms of tardive dystonia for the 2 years he smoked cannabis. In addition, we performed a comprehensive review of the literature regarding the use of cannabinoids to control dyskinesia.

References

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