

Ziprasidone and Tardive Dystonia: A Case Report and Literature Review

Aslı Bahar Turan¹, Cengiz Akkaya², Salih Saygın Eker², Aslı Sarandöl², Necdet Karlı²

ÖZET:

Ziprasidon ve tardif distoni: Bir olgu sunumu ve literatürün gözden geçirilmesi

Şizoafektif bozukluk tanısı alan 40 yaşındaki kadın hasta, 26 yaşından itibaren farklı tipik ve atipik antipsikotik ilaçlar ile izlenmiştir. Tedavisini kendi isteği ile kesen hastanın 3 ay sonra psikotik semptomlarında alevlenme olması üzerine ziprasidon ve valproik asit tedavisi başlanmıştır. Tedavinin 6. ayında servikal bölgede tardif distoni gelişmesi üzerine hastanın ziprasidon tedavisi kesildi, ancak yakınmaları devam etti. Distonik yakınmaları ve psikotik semptomları göz önünde bulundurularak 75 mg/gün klozapin tedavisi başlandı ancak yanıt alınamadı. Semptomlarda düzelme sağlanamaması ve hastanın yan etkilerden yakınması üzerine, klozapin dozu 25 mg/gün'e düşüldü ve botulinum toksini tip A uygulandı. Kısmi düzelme sağlanması üzerine botulinum enjeksiyonların tekrarı planlandı. Atipik antipsikotik ilaçların ekstrapiramidal yan etkileri tipik antipsikotiklerden daha az olsa da, kısıtlayıcı olabilen bu tür yan etkileri nedeniyle dikkatli olunmalıdır.

Anahtar sözcükler: Ziprasidon, tardif distoni, şizoafektif bozukluk

Klinik Psikofarmakoloji Bülteni 2011;21(3):242-5

ABSTRACT:

Ziprasidone and tardive dystonia: a case report and literature review

A 40-year-old woman with the diagnosis of schizoaffective disorder had been treated with different typical and atypical antipsychotic drugs since the age of 26. Three months after self-discontinuing her medication, she experienced an exacerbation of her psychotic symptoms, so ziprasidone and valproic acid treatment were started. Six months after initiation of the treatment, tardive dystonia was developed involving the neck region. Discontinuation of ziprasidone produced no benefit; thus clozapine, 75 mg/day, was initiated both for psychotic symptoms and dystonia. Due to lack of improvement in the dystonia and because she suffered from side effects, the dosage of clozapine was decreased to 25 mg/day and botulinum toxin type A treatment was administered. She had partial improvement and repeated injections were planned. Although atypical antipsychotic drugs cause fewer extrapyramidal side effects than typical antipsychotics, we must be cautious when prescribing these drugs because of their disabling side effects.

Key words: Ziprasidone, tardive dystonia, schizoaffective disorder

Bulletin of Clinical Psychopharmacology 2011;21(3):242-5

¹Department of Neurology, ²Department of Psychiatry, Uludag University Medical Faculty, Bursa -Turkey

Yazışma Adresi / Address reprint requests to: Cengiz Akkaya, Department of Psychiatry, Uludag University Medical Faculty, Bursa -Turkey

Elektronik posta adresi / E-mail address: cakkaya@uludag.edu.tr

Gönderme tarihi / Date of submission: 31 Aralık 2010 / December 31, 2010

Kabul tarihi / Date of acceptance: 30 Ocak 2011 / January 30, 2011

Bağıntı beyanı:

A.B.T., C.A., S.S.E., A.S., N.K.: Yazarlar bu makale ile ilgili olarak herhangi bir çıkar çatışması bildirmemişlerdir.

Declaration of interest:

A.B.T., C.A., S.S.E., A.S., N.K.: The authors reported no conflict of interest related to this article.

INTRODUCTION

Ziprasidone is an atypical antipsychotic agent with a higher affinity for serotonin (5-HT_{2A}) receptors than for dopamine (D₂) receptors (1). It also has activity as a 5-HT_{1A} receptor agonist and is a very weak inhibitor of serotonin and norepinephrine reuptake in vitro (2,3). Ziprasidone is approved for the treatment of schizophrenia, schizoaffective disorder, and acute manic or mixed episodes associated with bipolar disorder (4). It has relatively few side effects, including extrapyramidal side effects, which have been infrequently reported (3-5).

Tardive dystonia is a type of movement disorder that occurs as a delayed side effect in 0.4-4% of the patients

treated with dopamine receptor antagonists (6). It is characterized by generally slow and repetitive involuntary muscle contraction, which may affect the limbs, trunk, neck, face, or the whole body (7,8). When tardive dystonia involves the head and neck, it produces lateral collis, retrocollis, or anterocollis, causing disability.

Here, we report a female schizoaffective patient who developed tardive cervical dystonia after six months of ziprasidone treatment.

CASE REPORT

A 40-year-old woman had visual and auditory hallucinations and delusions of persecution and reference as



Picture 1: Retrocollis and right lateral collis before botulinum toxin type A injection.



Picture 2: Partial improvement after botulinum toxin type A injection.

initial manifestations of schizoaffective disorder at the age of 26. Different typical and atypical antipsychotic drugs (chlorpromazine, haloperidol, quetiapine, and zuclopenthixol) had been used for her treatment until 2009. There was no significant medical or family history, but she had a history of Parkinsonism and restless leg syndrome, which were diagnosed as a secondary movement disorder due to antipsychotic drugs; these adverse effects were temporary and disappeared after discontinuing the treatment. In 2009, three months after self-discontinuing her medication, she experienced an exacerbation of her psychotic symptoms. Treatment of ziprasidone at 80 mg/day and valproic acid at 500 mg/day had been started. During the six-month follow up, she had no extrapyramidal side effects, but after six months, dystonic posture and involuntary movements appeared in her neck region and she was referred to a neurology out-patient clinic. Neurological examination revealed retrocollis and right lateral collis; the other parts of the examination were normal, except for the dystonia. Laboratory tests were also within normal limits. She was diagnosed with tardive cervical dystonia. Ziprasidone was decreased to 20 mg/day, but the involuntary movements continued and were even exacerbated, so ziprasidone was discontinued and clozapine was started at 25 mg/day and increased to 75 mg/day, after two weeks with no improvement (Picture 1). She suffered from the side effects of clozapine, including increased heart rate, increased salivation, and tremors, so the dosage of clozapine was decreased to 25 mg/day and botulinum toxin type A was injected to the involved cervical muscles. Three weeks after the injection, retrocollis

improved but right lateral collis showed no improvement (Picture 2). Repeated injections with an increased dose of botulinum toxin type A were planned due to partial improvement while still on clozapine treatment (25 mg/day), which attenuated the psychotic symptoms. Informed consent for publication was obtained from the patient.

DISCUSSION

First-generation antipsychotics, also known as typical antipsychotics, are effective drugs but because of their extrapyramidal side effects, they have fallen out of favor. In the 1980s, second generation (or atypical) antipsychotics that cause fewer extrapyramidal side effects were developed (5). Ziprasidone is the fifth atypical antipsychotic that was approved in 2001 (3). It has been shown to cause mild or moderate extrapyramidal side effects in 4.7% of patients; typical antipsychotics cause side effects in 40-85% of patients (4,9).

Tardive syndromes are persistent, drug-induced movement disorders that result from postsynaptic supersensitivity induced by sustained inhibition of dopaminergic neurotransmission (10). Because atypical antipsychotics such as ziprasidone have less affinity for dopamine receptors, they have the advantage of having low risk for tardive syndrome side effects. In the literature, there are only four reports of tardive dystonia caused by ziprasidone. Here, we present the fifth patient with tardive dystonia after six months of ziprasidone treatment. The four previously reported cases are presented in detail in Table 1.

Table 1: Cases of tardive dystonia caused by ziprasidone

Published in	Age, Gender	Concomitant disease	Family history	Previous EPS symptoms	Diagnosis	Treatment duration	Dosage	Localization of symptoms	Treatment	Response to treatment
2005 (11)	56, F	-	-	-	Migraine	11 months	80 mg/day	Tongue, jaw	Discontinued+ botulinum toxin type A injections	Without success
2008 (12)	25, M	-	Obsessive compulsive disorder, dysthymia	-	Paranoid Schizophrenia (schizo-obsessive-compulsive type)	6–8 weeks	120 mg/day	Trunk	Discontinued	Success
2008 (13)	39, F	-	-	Oculogyric crisis	Paranoid schizophrenia	8 months	120 mg/day	Larynx, vocal cord	Discontinued	Success
2009 (14)	50, F	Autoimmune thyroiditis	-	-	Atypical depression	4 months	80 mg/day	Neck	Discontinued+ Clonazepam 150 mg/day+ botulinum toxin type A injections	Success
2010	40, F	-	-	Parkinson's disease, restless leg syndrome	Schizoaffective disorder	6 months	80 mg/day	Neck	Discontinued+ Clonazepam 75 mg/day+ botulinum toxin type A injections	Partial success

This case differs from the other four cases (paranoid schizophrenia, atypical depression, migraine) with the diagnosis of schizoaffective disorder (11–14). The dystonic symptoms appeared at 4–11 months in three cases (11,13,14) and at 6 months in this case. Tibrewal et al. (12) reported early manifestations of dystonic symptoms at six to eight weeks.

This is the second case report presenting tardive dystonia involving the neck region. The first case was reported by Kutlu et al. in a depressive patient (14). Dystonia was improved with the discontinuation of ziprasidone treatment in two cases (12,13), but discontinuation of ziprasidone treatment did not improve dystonia in the other two cases in which botulinum toxin type A was administered (11,13). One patient improved with botulinum toxin type A treatment (14), while the other did not (11). Kutlu et al. administered botulinum toxin type A treatment following unsuccessful treatment with clozapine (14) as we did in the present case. Due to partial improvement, repeated injections are planned in our case. Although the use of clozapine is a good choice in the prevention and treatment of tardive dystonia, botulinum toxin A is currently thought to be the most effective

medical treatment for cervical dystonia and to be more effective than oral medications (15,16). There are, however, patients who have no response to botulinum toxin therapy (17).

Risk factors of neuroleptic-induced extrapyramidal symptoms include younger age, longer duration of neuroleptic exposure, and positive family history, but none are specific to tardive dystonia (18). Among the five cases including the present one, only one case had a positive family history of psychiatric disorders (obsessive compulsive disorder and dysthymia) and only one case was young (age 25) (12). This case is not a young patient and she has no positive family history, but she has a 14-year history of neuroleptic exposure.

Tsai et al. reported a history of oculogyric crisis with previous antipsychotic medications in their patient before the development of tardive dystonia (13). Since previous antipsychotic treatments caused Parkinsonism and restless leg syndrome in the present case, a history of extrapyramidal side effects may be a cautionary sign for dystonia.

The possibility of dystonia secondary to a pharmacodynamic interaction between valproic acid and ziprasidone could not be absolutely excluded in this case

because the patient also received treatment of valproic acid with ziprasidone as a mood stabilizer, and there are case reports supporting this kind of interaction in the literature (19,20). The possibility of primary dystonia can also not be absolutely excluded, although the Naranjo adverse drug reaction probability scale indicated a probable relationship (score: 5) between dystonia and ziprasidone (21).

References:

- Seeger TF, Seymour PA, Schmidt AW, Zorn SH, Schulz DW, Lebel LA, et al. Ziprasidone (CP-88,059): a new antipsychotic with combined dopamine and serotonin receptor antagonist activity. *J Pharmacol Exp Ther* 1995;275(1):101-13.
- Schmidt AW, Lebel LA, Howard HR Jr, Zorn SH. Ziprasidone: a novel antipsychotic agent with a unique human receptor binding profile. *Eur J Pharmacol* 2001;425(3):197-201.
- Caley CF, Cooper CK. Ziprasidone: the fifth atypical antipsychotic. *Ann Pharmacother* 2002;36(5):839-51.
- Greenberg WM, Citrome L. Ziprasidone for schizophrenia and bipolar disorder: a review of the clinical trials. *CNS Drug Rev* 2007;13(2):137-77.
- Mathews M, Muzina DJ. Atypical antipsychotics: new drugs, new challenges. *Cleve Clin J Med* 2007;74(8):597-606.
- Agarwal PA, Ichaporia NR. Flupenthixol-induced tardive dystonia presenting as severe dysphagia. *Neurol India* 2010;58(5):784-5.
- Aggarwal A, Jiloha RC. Olanzapine induced tardive dystonia. *Indian J Pharmacol* 2008;40(5):237-8.
- Duggal HS, Mendhekar DN. Clozapine-induced tardive dystonia (blepharospasm). *J Neuropsychiatry Clin Neurosci* 2007;19(1):86-7.
- Peacock L, Solgaard T, Lublin H, Gerlach J. Clozapine versus typical antipsychotics. A retro- and prospective study of extrapyramidal side effects. *Psychopharmacology (Berl)* 1996;124(1-2):188-96.
- Stahl SM, Davis KL, Berger PA. The neuropharmacology of tardive dyskinesia, spontaneous dyskinesia, and other dystonias. *J Clin Psychopharmacol* 1982;2(5):321-8.
- Papapetropoulos S, Wheeler S, Singer C. Tardive dystonia associated with ziprasidone. *Am J Psychiatry* 2005; 162(11): 2191.
- Tibrewal P, Zutshi A, Math SB. Tardive dystonia and ziprasidone: a case report. *Prim Care Companion J Clin Psychiatry* 2008;10(1):71-2.
- Tsai CS, Lee Y, Chang YY, Lin PY. Ziprasidone-induced tardive laryngeal dystonia: a case report. *Gen Hosp Psychiatry* 2008;30(3):277-9.
- Kutlu A, Dündar S, Altun NS, Budak F. Ziprasidone induced tardive cervical dystonia. *Psychopharmacology Bulletin* 2009 42(4): 64-8.
- Raja M. Managing antipsychotic-induced acute and tardive dystonia. *Drug Saf* 1998;19(1): 57-72.
- Brans JW, Lindeboom R, Snoek JW. Botulinum toxin versus trihexyphenidyl in cervical dystonia: a prospective, randomized, double-blind controlled trial. *Neurology* 1996;46 (4):1066-72.
- Jankovic J. Botulinum toxin in clinical practice. *J Neurol Neurosurg Psychiatry* 2004;75(7):951-7.
- Lencer R, Eismann G, Kasten M, Kabakci K, Geithe V, Grimm J, et al. Family history of primary movement disorders as a predictor for neuroleptic-induced extrapyramidal symptoms. *Br J Psychiatry* 2004 185: 465-71.
- Habermeyer B, Rabovsky K, Jentzsch C, Pinhard K, Müller-Spahn F. Cervical dystonia due to interaction of valproic acid and quetiapine. *J Clin Psychopharmacol* 2007;27(4):396-7.
- Yohanan M, Aulakh JS, Weith J, Hawkins JW. Pisa syndrome in a patient in a wheelchair taking valproic acid. *Am J Psychiatry* 2006;163(2):325-6.
- Naranjo CA, Busto U, Sellers EM, Sandor P, Ruiz I, Roberts EA, et al. A method for estimating the probability of adverse drug reactions. *Clin Pharmacol Ther* 1981;30(2):239-45.

CONCLUSION

Although atypical antipsychotic drugs cause fewer extrapyramidal side effects than typical antipsychotics, there is always a risk for tardive dystonia with ziprasidone use that should be kept in mind by clinicians. Caution should be exercised when prescribing these drugs because of this disabling side effect. Botulinum toxin may be a good choice of it's treatment.