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Efficacy of Low-dose Pramipexole Augmentation in the Treatment of Refractory Psychotic Depression Complicated with Tardive Dyskinesia: A Case Report

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ÖZET:

Tedaviye dirençli psikotik bulgulu depresyon ve tardiv diskinezide düşük doz pramipeksol eklenmesiyle görülen düzelme: Bir olgu sunumu

Tardiv Diskinezi (TD) antipsikotiklerin ciddi bir yan etkisidir. Pramipeksol dopamin D3 reseptör agonisti etkisi ile TD tedavisinde etkili olabilir. Bipolar depresyon ve tedaviye dirençli depresyonda (TDD) yapılan çalışmalar, pramipeksol'ün antidepresan etkisini desteklemektedir. Bu yazıda; depresyon tedavisi için 2,5 yıldır çeşitli antidepresan, anksiyolitik ve antipsikotik ilaçlar kullanan, 55 yaşında bir kadın olgu sunulmuştur. Uygulanan tedaviler ile olguda depresyon kısmen düzelse de relapslar önlenememiştir. Olgu, çenede ve ayaklarda beliren istemsiz hareketler ve işlevsellikte belirgin azalma medemiyle TD ve TDD tanıları ile kliniğimize yatırılmıştır. 6 aylık tedavi boyunca çeşitli antidepresan, anksiyolitik ve antipsikotikler etkin doz ve sürelerde kullanılmıştır. Depresyon kısmen düzelmiş, hipokondriyak sanrılar ve diskinezi düzelmemiştir. Yatışının son ayında sertralin 200 mg/gün, amitriptilin 60 mg/gün, klonezepam 2 mg/gün, biperiden 4 mg/gün kombinasyonuna 0.125 mg/gün pramipeksol eklenmiştir. 4. haftada depresyon ve diskinezi düzelmiş, hasta taburcu edilmiştir. 8 aylık izlemde relaps ya da rekürrens gözlenmemiştir. Pramipeksol TDD ve TD'de ekleme tedavisi olarak umut vaat etmektedir.

Anahtar sözcükler: Pramipeksol, depresyon, psikotik, diskinezi, ilaca bağlı

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ABSTRACT:

Efficacy of low-dose pramipexole augmentation in the treatment of refractory psychotic depression complicated with tardive dyskinesia: a case report

Tardive dyskinesia (TD) is a severe complication of antipsychotic treatment. Pramipexole can be effective in the treatment of TD due to its D3 dopamine receptor agonist effect. Studies conducted in bipolar depression and treatment-resistant depression (TRD), support the antidepressant effect of pramipexole. Here we present the case of a 55 year-old female. For the treatment of depression, she received antidepressants, anxiolytics and antipsychotics for 2.5 years. When severe bruxism, fidgeting, and serious functional impairment emerged, she was re-hospitalized and diagnosed with TRD and TD. Several combinations of antidepressants, anxiolytic, and antipsychotics were administered. The depression improved partially, but hypochondriac preoccupations and dyskinesia persisted. At the sixth month, pramipexole 0.125 mg/day was added to sertraline 200 mg/day, amitriptyline 60 mg/day, clonazepam 2 mg/day, and biperiden 4 mg/day. The depression and dyskinesia improved and she was discharged. TRD and TD improved within the first 4 weeks of pramipexole administration and no relapse was observed. Pramipexole is a promising agent in the treatment of TRD and TD.

Key words: Pramipexole, depression, psychotic, dyskinesia, drug-induced

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INTRODUCTION

Treatment-resistant depression (TRD) is defined as a major depressive episode which does not respond to adequate treatment (1). Multiple strategies for the treatment of TRD have been investigated in clinical trials (2). However the data on longer-term strategies of continuation and maintenance therapy in patients with TRD are much more sparse.

Tardive dyskinesia (TD) is a severe and potential irreversible side effect of antipsychotic treatment. It is characterized by abnormal, involuntary movements of the mouth, face, trunk, and limbs (3).

A patient, who was diagnosed with TRD with TD and who responded to low-dose pramipexole augmentation, is presented and the role of pramipexole augmentation in the treatment of TRD with TD is discussed.

CASE REPORT

Here we present the case of a 55 year-old female patient treated for depression for 3 years. All interventions on this

case were conducted in accordance with the Declaration of Helsinki. All procedures were carried out with the informed written consent of the patient. The patient reported that; she had received a combination of citalopram 40 mg/day, chlorpromazine 100 mg/day, imipramine 75 mg/day, trazodone 100 mg/day and quetiapine 25 mg/day for the first 4 months of her treatment. She was hospitalized for a period of 3 weeks when it was concluded that she was unresponsive to treatment. During the hospitalization period she was administered sertraline 150 mg/day, quetiapine 25 mg/day and alprazolam 1 mg/day and was discharged when partially improved. After 3 months of regular treatment she was re-hospitalized with a relapse of her depression. This time she was administered fluvoxamine 200 mg/day and olanzapine 20 mg/day, to which she didn't respond well. After discharge her medications had been switched to escitalopram 40 mg/day, mirtazapine 15 mg/day and amitriptyline 75 mg/day. Following this switch, severe bruxism, fidgeting, and serious functional impairment emerged and she was transferred to the Ege University Department of Psychiatry.

On the first visit depressive mood, anhedonia, severe anxiety, apathy, hypomimia, global insomnia, loss of spontaneous attention, deficit in short term memory, anergy, hypochondriacal preoccupations, somatic delusions, bradykinesia, chewing-like stereotypic movements of the jaw and fidgeting of the feet were detected. The Extrapyramidal Symptom Rating Scale score for the patient was 15 (Parkinsonism and dystonia: 1; Parkinsonism examination: 4; Tremor: 1; Dyskinesia: 5). She was administered biperiden 6 mg/day after being diagnosed with drug induced tardive dyskinesia by the neurologist.

The patient refused electro-convulsive treatment for her refractory depression. Thus, she was administered amitriptyline (25-200 mg/day), olanzapine (5-20 mg/day) and clonazepam 2 mg/day combination therapy (all drugs were titrated up gradually within 10 weeks) for TRD with psychotic features. Olanzapine was discontinued since somatic delusions remained the same and dyskinesia deteriorated.

Amitriptyline was discontinued after 10 weeks of treatment. Clomipramine was started (titrated-up to 225 mg/day) and combined with folic acid 10 mg/day, omega-3 600 mg/day, vitamin E 600 IU/day, clonazepam 2 mg/day and biperiden 4 mg/day. She did not improve at the end of six weeks on this regimen. Clomipramine was switched to sertraline (150 mg/day) and combined with amitriptyline 60 mg/day. After six weeks her depression improved partially but hypochondriacal preoccupations and dyskinesia remained unchanged. At the sixth month of hospitalization, pramipexole was added to the therapy for its anti-dyskinetic and antidepressant features.

At the end of 4 weeks, her depressive symptoms and dyskinesia improved with pramipexole 0.125 mg/day combined with sertraline 200 mg/day, amitriptyline 60 mg/day, clonazepam 2 mg/day, biperiden 4 mg/day, vitamin E 600 IU/day, Omega-3 600 mg/day and the patient was discharged. She was followed up at the outpatient clinic and found to be improved fully at the end of 3 months. After 8 weeks her Hamilton Depression Rating Scale score dropped to 13, from a score of 35 on the first visit. The Extrapyramidal Symptom Rating Scale score dropped to 9 after 4 weeks of pramipexole augmentation from 15 at the beginning of treatment.

DISCUSSION

The residual symptoms did not improve and relapses occurred in this TRD case even though she was treated with effective doses and for adequate durations. The depressive symptoms and TD improved within the first 4 weeks of low-dose (0.125 mg/day) pramipexole administration, whereas relapse or recurrence was not observed during long-term follow-up (6 and 8 months, respectively).

Recent genetic and pharmacological studies indicate the role of the dopamine D3 receptor in TD (4). Pramipexole, a synthetic aminothiazole derivative, has a full agonist effect on dopamine receptors. It was proposed that pramipexole could be effective in the treatment of TD due to its D3 dopamine receptor agonist effect (4-5). Results from animal studies indicate the role of the dopamine D3 receptor in TD (4).

Rehor et al. also reported a 21 year-old-male patient with severe oro-facial TD who responded well to pramipexole augmentation (1.44 mg/day) combined with clozapine, valproic acid, oxazepam, bornaprin hydrochloride and tiapride. The patient showed better concentration on his work with no side effects (5).

It is proposed that pramipexole may improve depression in patients with Parkinson's disease along with its neuro-

protective effect (6-7).

Studies conducted with bipolar depression and TRD patients support the antidepressant effect of pramipexole. In a study including 174 non-psychotic unipolar depression patients, pramipexole 1.0 mg/day and fluoxetine for a period of 8 weeks were more effective than placebo (8). Open studies report 40-50% response rates with pramipexole addition to mood stabilizers or antidepressants in the treatment of TRD patients (9-13). Pramipexole augmentation of antidepressant treatment was found to be relatively safe and presumably effective in a 1 year follow-up of TRD patients (14). It is reported that pramipexole is also effective in the treatment of bipolar depression (15) and is a promising agent in the treatment of bipolar depression.

CONCLUSION

Pramipexole, with its different pharmacodynamic and pharmacokinetic properties, is a promising agent in the treatment of TRD and TD. Augmentation of antidepressants and antipsychotics with pramipexole could be considered as a safe combination strategy with its low plasma binding properties and mild side effect profile.

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