

Paliperidone ER-induced Tardive Dyskinesia

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ÖZET:

Paliperidon ER bağlı geç diskinezi

Kanıtlar atipik antipsikotik kullanımının daha az geç diskinezi oluşturduğunu öne sürmektedir. Biz iki geç diskinezi olgusu sunmaktayız. Olgularımızda geç perioral diskinezi, paliperidon ER kullanımının 9. ve 12. aylarında gelişmiştir (sırasıyla 12 mg/gün ve 9 mg/gün dozlarında). Bu semptomlar birinci olguda ketiapin 800 mg/gün kullanımına değiştirilerek, ikinci olguda ise paliperidon dozunun 6 mg/gün'e azaltılması ile iyileşmiştir. Atipik antipsikotikler hareket bozuklukları ile ilişkili düşük riskli olarak bilinmesine rağmen paliperidon kullanımı ile bu yan etki gözlemlenmektedir.

Anahtar sözcükler: Geç diskinezi, şizofreni, paliperidon, ketiapin

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ABSTRACT:

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The evidence suggests a lower tardive dyskinesia risk associated with atypical antipsychotics. We present two adult female cases with tardive dyskinesia. Tardive perioral dyskinesia developed in patients at the ninth and twelfth months of paliperidone ER treatment (12 mg/day and 9 mg/day, respectively). These symptoms were improved after switching to quetiapine 800 mg/day in the first patient while lowering the dose of paliperidone ER to 6 mg/day resulted in significant improvement in the second patient. Although atypical antipsychotics have a low risk for movement disorder related events, paliperidone ER does not seem to be lacking in such adverse effects.

Key words: Tardive dyskinesia, paliperidone, schizophrenia, quetiapine

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INTRODUCTION

Tardive dyskinesia (TD) is generally accepted as the most severe extrapyramidal adverse effect of antipsychotic treatment that is usually associated with long-term antipsychotic treatment with higher dosages, female gender, co-morbid affective symptoms and greater severity of the psychotic disorder (1). To meet the criteria of TD, the symptoms must develop after at least 3 months of exposure to a dopamine antagonist or within 4 weeks of withdrawal and should be present at least 4 weeks (2). Different neurochemical hypotheses had been related to the development of tardive dyskinesia, including dopaminergic

hypersensitivity, disturbed balance between dopaminergic and cholinergic systems, dysfunctions of striatonigral GABAergic neurons and excitotoxicity (3).

The evidence suggests a lower TD risk for second-generation antipsychotics (SGAs) than for first-generation antipsychotics (FGAs) (4). Paliperidone ER, 9-hydroxyrisperidone, is the first SGA that is an active metabolite of another SGA, its parent compound, risperidone. Using the active metabolite as a pharmacological agent may have advantages over using the parent compound, for example decreasing particular adverse reactions (5). Nowadays, there has been a recent, unique case that was reported in relation with TD and

paliperidone ER use (4). In this study, we present two cases with TD after paliperidone ER treatment in patients with schizophrenia.

CASE REPORTS

Case 1

Miss Z, female, 21 years-old, living with her family. She was admitted to our outpatient clinic with complaints of thought controlling, commanding her mind and involuntary perioral movements. Seven years before, she had experienced withdrawal, staying at home all the time, difficulties in academic success, and delusional perception with a diagnosis of major depression with psychotic features. Fluoxetine 20 mg/day had been started for 8 weeks. However, it had been replaced with clomipramine 75 mg/day titrating up to 225 mg/day because of resistant symptoms such as anhedonia, avolition, isolation, delusional perception and functional impairment. Olanzapine 10 mg/day had been initiated after the diagnosis had been changed as NOS psychotic disorder. She was non-adherent to her treatment regimen because of significant weight gain and was reluctant to use antipsychotic agent. After six months, in follow up visits auditory hallucinations and persecution delusions were detected. She was diagnosed as schizophrenia according to the DSM IV-TR and paliperidone ER 6 mg/day was prescribed and titrated up to 12 mg/day in four months. She had better interpersonal relationships, lesser anhedonia but resistant delusions of thought control. Due to the perioral dyskinetic movements while she was taking paliperidone ER 12 mg/day treatment for nine months the patient was internalized. Her dyskinesia score according to the Extrapyramidal Symptom Rating Scale (ESRS) was 20. By cross tapering, quetiapine treatment up to 800 mg/day was started, paliperidone ER was discontinued, and vitamin E 1200 MU/day was added in the existing therapy. The perioral dyskinesia was improved after this treatment regimen for one month and the ESRS score was 10 points, although there was no clear improvement clinically.

Case 2

Miss A, female, 24 years-old, living with her family. She was admitted to the outpatient clinic with complaints of abnormal movements in the jaw joint and involuntary tongue and mouth movements while she was taking 9 mg/day paliperidone ER treatment for one year. She had a history of schizophrenia diagnosis with the symptoms of insomnia, auditory commanding hallucination, somatic delusion, social isolation, social and occupational dysfunction two years before and she was non-compliant to the treatment regimen of 10 mg/day olanzapine. In mental and physical examinations, she demonstrated frequent protrusion of the tongue, a large amplitude opening movement of the jaw, and a slight puckering of the mouth; her ESRS score was 18 and negative symptoms of schizophrenia such as affective flattening and social withdrawal were detected. The paliperidone ER dose was reduced to 6 mg/day and 1 mg/day clonazepam was added to therapy for perioral dyskinesia; her ESRS score was reduced to 12 after 1 month.

DISCUSSION

In the dopamine supersensitivity hypothesis, the blockade of striatal D2 receptors by antipsychotic drugs leads to their up-regulation resulting in overactivity of the striatal dopaminergic system that may present as TD (6). In the SOHO study which was a prospective and observational study of outcomes in schizophrenia treatment, other than typical antipsychotics, the risperidone cohorts had a significantly higher risk of TD (2.7 fold higher) development compared to olanzapine (7). Paliperidone ER has shown more potent occupancy at the dopamine D2 receptor than risperidone (8). In the literature, there have been three cases of abnormal movements related to paliperidone ER: a report of TD related to paliperidone ER use (4), development of choreo-athetotic movements after paliperidone ER withdrawal (9) and rabbit syndrome after paliperidone ER use (9); thus, paliperidone ER

should be considered as a potential contributor in the development of TD in the current two cases. In addition, paliperidone ER at doses of 9 mg or greater has more significant risk for movement disorder related adverse events (10,11) and lowering the dose of paliperidone ER leads to improvement in TD (3). In this study, one patient was on 12 mg/day paliperidone ER treatment and the second patient was on 9 mg/day treatment and the doses were highly related to adverse movement symptoms. In addition, besides clonazepam treatment, lowering the paliperidone ER dose to 6 mg/day in the second case might also support the role of paliperidone ER in the development of TD. In the literature, use of the agent at lower doses is related to fewer risk of tardive dyskinesia if cessation of that drug is clinically contraindicated; therefore we reduced

the dosage in the second case (12). Another strategy for TD induced by atypical antipsychotics in patients with schizophrenia is to switch the antipsychotic to another atypical agent as reported in the successful treatment of two cases with olanzapine associated TD after switching to quetiapine (2,13) and some research has supported vitamin E treatment for tardive dyskinesia especially at a dose of 1600 IU (14) and clonazepam about 4 mg/day (15) hence we used these agents in the treatment of our cases.

In conclusion, although paliperidone ER is a novel drug as an atypical antipsychotic with lower risk of extrapyramidal effects, it does not seem lacking in movement disorder related adverse effects. By presenting the current cases, we aimed to draw the attention of clinicians to the possibility of TD associated with the use of paliperidone ER.

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