

Improvement of Tardive Dyskinesia after Switching from Zuclopenthixol Decanoate to Paliperidone Palmitate: a Case Report

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ABSTRACT

Improvement of tardive dyskinesia after switching from zuclopenthixol decanoate to paliperidone palmitate: a case report

Long-acting injectable (LAI) antipsychotics are an effective option in schizophrenia that increase treatment adherence in potentially non-compliant patients. Tardive dyskinesia is a potentially treatment-resistant movement disorder that can be a problem after long-term antipsychotic use. Atypical antipsychotics with long-acting formulations offer a safer option for acute extrapyramidal side effects, but their effect in tardive dyskinesia is not clear. We report a case of tardive dyskinesia of the perioral area and the tongue after long-term use of zuclopenthixol decanoate, a LAI antipsychotic is a potent dopamine (D2) receptor antagonist. The patient was a 45-year-old Caucasian male with a 25-year history of schizophrenia who was using olanzapine and zuclopenthixol decanoate at the index consultation when the dyskinesia was recognized. Chlorpromazine, haloperidol, olanzapine, and quetiapine were the antipsychotics that had been used for differing periods in addition to zuclopenthixol decanoate over the last six months, before the emergence of tardive dyskinesia. The Abnormal Involuntary Movements Scale was used in scoring the oropharyngeal dyskinesia. Because of the patient's former non-compliance with oral medication and concerns of treatment adherence, we planned to continue using LAI. After switching to paliperidone palmitate, a second generation LAI with receptor-antagonist effects for dopamine (D2), serotonin (5HT-2), and noradrenaline (NE-alpha2) receptors, we observed the improvement of the tardive dyskinesia.

Keywords: Long-acting injectable antipsychotics, paliperidone palmitate, schizophrenia, tardive dyskinesia, zuclopenthixol

ÖZ

Zuklopentiksol dekanooattan paliperidon palmitata geçiş sonrasında tardiv diskinezi düzelmeye: Bir olgu sunumu

Uzun etkili enjektabl antipsikotikler şizofrenide etkili bir tedavi seçeneğidir ve ilacı bırakma potansiyelinin yüksek olduğu hastalarda tedavi uyumunu artırmaktadır. Tardiv diskinezi, uzun süre antipsikotik kullanımı sonrasında sorun olabilen tedavi edilmesi zor bir hareket bozukluğudur. Uzun etkili formları olan atipik antipsikotikler akut ekstrapiramidal yan etkiler için daha güvenli bir seçenek olmalarına karşın, tardiv diskinezideki etkileri net değildir. Güçlü dopamin (D2) reseptör antagonisti özelliği bulunan uzun etkili enjektabl bir antipsikotik olan zuklopentiksol dekanooatın uzun süre kullanımı sonrası gelişen, perioral ve dil bölgesinde tardiv diskinezi olan bir olguyu bildirmektediriz. Yirmi beş yıllık şizofreni öyküsü bulunan, 45 yaşındaki beyaz erkek hasta, tardiv diskinezi fark edildiği zaman olanzapin ve zuklopentiksol dekanooat kullanmaktaydı. Son 6 ayda zuklopentiksol dekanooatla beraber çeşitli aralıklarla klorpromazin, haloperidol, olanzapin ve ketiapin kullanımı da olmuştu. Otofarijyal diskineziyi ölçmekte Anormal Hareket Bozuklukları Ölçeği kullanıldı. Geçmişte oral tedavi ile tedavi uyumsuzluğu öyküsü bulunduğu uzun etkili enjektabl antipsikotik kullanımına devam etmeyi planladık. İkinci kuşak uzun etkili enjektabl antipsikotiklerden olan ve dopamin (D2), serotonin (5HT-2), noradrenalin (NE-alfa2) reseptörlerinde antagonist etkisi olan paliperidon palmitat olarak antipsikotik tedavisi değiştirildikten sonra, tardiv diskinezi düzelmeye gözlemledik.

Anahtar kelimeler: Uzun etkili enjektabl antipsikotikler, paliperidon palmitat, şizofreni, tardiv diskinezi, zuklopentiksol



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INTRODUCTION

Tardive dyskinesia (TD) is a serious and usually treatment-resistant adverse effect of long-term use of antipsychotics drugs. Lip smacking, chewing, protrusion of tongue, choreiform hand movements, and in severe cases pelvic thrusting can be seen as forms of TD. Severe orofacial movements can lead to problems in speaking, eating, and breathing, and they are also associated with poor quality of life, non-adherence, and increased medical morbidity and mortality (1,2). Although TD is reported to occur with the use of anticholinergics, antidepressants, lithium, calcium channel blockers, and several other agents, antipsychotics are usually responsible for the majority of cases (2,3). The mechanism of TD is poorly understood, but it is thought to be the dopamine receptor super-sensitivity due to long-term blockade of dopamine receptors (4). Increasing age, female sex, affective disorders, metabolic diseases such as diabetes mellitus, organic brain dysfunction, acute extrapyramidal symptoms (EPS) and concomitant use of anticholinergic agents are the most important risk factors for TD (5). Risk of TD is reported to be lower in second-generation antipsychotics (SGA) than first-generation antipsychotics (FGA) (4). Reported ratios for tardive dyskinesia were 13.1% for atypical antipsychotics and 32.4% for first-generation antipsychotics (6).

Paliperidone (9-hydroxyrisperidone), which is the active metabolite of risperidone, is an SGA with receptor antagonist effects on dopamine (D₂), serotonin (5-HT₂), and noradrenaline (NE alpha-2) receptors, and since it binds to D₂ receptors less tightly, it has a lower risk of acute EPS than risperidone (7,8). On the other hand, because of the D₂ receptor antagonist effect, it still has a risk of TD by upregulating the striatal dopaminergic system (9). Paliperidone palmitate, the once-monthly long-acting injectable (LAI) form of paliperidone, has a half-life of 25-49 days and it is approved in the treatment of schizophrenia (10). LAI antipsychotics cause little fluctuation in blood concentrations of the drug and provide continuously effective blood levels in

comparison to oral antipsychotics, but they also constitute the risk of TD. The rates of TD are lower in SGA-LAI than FGA-LAI (11-13).

Zuclophenthixol is a potent D₂ receptor-blocking FGA and zuclophenthixol decanoate is the available LAI formulation that is commonly used in schizophrenia in a twice-monthly dosage (14). It is reported to be slightly more effective in preventing relapses than other FGA-LAI, but this is at the expense of increased side effects, as it has a potentially high risk of TD (15).

We report a case of a patient with TD that occurred while using zuclophenthixol decanoate. Improvement in dyskinetic movements was observed after changing from zuclophenthixol decanoate to paliperidone palmitate. The effectiveness of antipsychotics except clozapine and quetiapine in the management of TD is very rare dealt with in the literature (16-19).

CASE

The patient was a 45-year-old Caucasian man with a 25-year history of schizophrenia. In the past, he had undergone numerous psychiatric hospitalizations in different hospitals with the indication of refusal of treatment and homicidal risk. The interepisodic clinical outcome was not good, showing repetitive poor compliance with outpatient medications.

He was hospitalized for refusal of treatment and homicidal risk with delusions of persecution and auditory hallucinations. His psychomotor activity was increased and there were neither signs of a mood disorder nor any other medical condition that might require clinical attention. During hospitalization, he was first treated with olanzapine 20mg/day, quetiapine 100mg/day, and biperiden 4mg/day. Haloperidol 20mg/day intramuscularly was added for aggressive excitations for 10 days. Zuclophenthixol decanoate, which the patient had been using improperly before the hospitalization, was also continued. Before the hospitalization, he was occasionally accepting the zuclophenthixol injections during outpatient consultations. Two weeks after admission, haloperidol was changed to chlorpromazine 100mg/day and quetiapine 25mg/day was used as an adjunct for

Table 1: Changes in the severity of tardive dyskinesia during the follow-up period

Abnormal Involuntary Movements Scale	1.week	2.week	3.week	4.week
Muscles of facial expression	0	0	0	0
Lips and perioral area	3	2	1	0
Jaw	0	0	0	0
Tongue	3	2	1	0
Upper extremity	0	0	0	0
Lower extremity	0	0	0	0
Neck, shoulder and hips	0	0	0	0
Severity of abnormal movements	3	2	1	0
Incapacitation due to movements	1	1	0	0
Patient's awareness	2	0	0	0
Current problem with teeth	No	No	No	No
Are dentures usually worn	No	No	No	No
Edentia	No	No	No	No
Do movements disappear with sleep	Yes	Yes	Yes	Yes

insomnia. Biperiden was also used continuously because of the relief of mild antipsychotic-induced parkinsonism which re-occurred in the attempts of stopping anticholinergic treatment. After relief from persecutory delusions and auditory hallucinations, he was discharged with a treatment regimen of olanzapine 20mg/day, biperiden 4mg/day orally and zuclopenthixol decanoate 200mg bimonthly intramuscularly.

Oropharyngeal dyskinesia of the tongue, lips, and the perioral area were first observed during outpatient consultations while the patient was using olanzapine 20mg/day, biperiden 4mg/day and zuclopenthixol decanoate 200mg bimonthly. The Abnormal Involuntary Movements Scale (AIMS) was used weekly to score the TD, and an AIMS score of 12 was recorded on the first day that the dyskinesia was observed. Changes in the scores of this scale are shown in Table 1.

Olanzapine was discontinued and a switch from zuclopenthixol decanoate to paliperidone palmitate was made. On the day of the LAI antipsychotic administration, paliperidone palmitate 150mg was injected intramuscularly and the treatment regimen was changed to paliperidone palmitate 150mg monthly with biperiden 4mg orally continued. Weekly improvement in TD was observed with complete resolution in the 4th week. Attempts to stop biperiden failed because of the emergence of mild symptoms of

parkinsonism when biperiden was stopped. After one year follow-up, there were no signs of oropharyngeal or any other kind of dyskinesia, and the patient was clinically stable on continuous treatment with paliperidone palmitate.

DISCUSSION

In our patient, the occurrence and of antipsychotic-induced parkinsonism, which was relieved by biperiden, constituted a risk factor for TD. When involuntary dyskinetic oropharyngeal movements occurred, the patient was using zuclopenthixol, olanzapine, and biperiden. Even though there are peculiar cases of TD induced by olanzapine, especially pronounced in the geriatric population, the probability of zuclopenthixol being responsible for the oropharyngeal dyskinesia is higher because LAI FGAs have very high risk of TD (20-24). There are reported cases of paliperidone palmitate-induced tardive dyskinesia, tardive dystonia, and persistent EPS (25-29). In a recent research, the incidence of TD with paliperidone palmitate is reported as 13.1% in the first month and 5.4% in months 6-7, declining over time (13).

Since paliperidone binds less tightly to dopamine D2 receptors and causes less EPS than the FGAs and the parent compound, risperidone, it can be suggested that it has a lower risk of TD (7,8). There is an

interesting case reported involving improvement in oral dyskinesia after switching from aripiprazole to paliperidone (oral), but the case we present here is the first one in the literature with improvement in tardive dyskinesia after moving to paliperidone palmitate (18).

In our case, after the emergence of TD, one reliable option would have been to decrease the dose of the current antipsychotic or switching to clozapine, but the previous history of non-compliance with oral medication and increase in adherence to treatment with LAI in this patient motivated us to continue the treatment with SGA-LAI (2). There are very well replicated studies the literature showing that LAI antipsychotics reduce the risk of relapse (30).

Switching from zuclopenthixol decanoate 200mg bimonthly to paliperidone palmitate 150mg monthly represents an increase in the antipsychotic dose when we compare the chlorpromazine-equivalent doses of the two antipsychotics: zuclopenthixol 100mg/week = chlorpromazine 100mg/day, but paliperidone 150mg/month = chlorpromazine 400mg/day (31). This may be the reason why the patient was still clinically stable without concomitant use of olanzapine, which he needed previously.

As there can be spontaneous remission in TD, it is difficult to suggest that paliperidone palmitate worked as a treatment for involuntary movements in our case (13). Some of the researchers use the Schooler-Kane standardized research criteria for TD between probable and persistent TD (32). At least 3 months of

cumulative exposure to neuroleptics, absence of other conditions that may be the cause of involuntary movements, and at least moderate dyskinetic movements (AIMS point 3 or more) in one body area or mild dyskinetic movements (AIMS point 2 or more) in two body areas are the requirements to meet these criteria. Three months of having an AIMS score fulfilling the criteria corresponds to probable tardive dyskinesia, and an additional 3 months of qualification is necessary for persistent TD. According to these criteria, TD in our case did not qualify for the persistent type, since we made changes in the antipsychotic medication of the patient before the duration criteria for persistent tardive dyskinesia were fulfilled. But with reference to our observation of improvement in TD after switching to paliperidone palmitate, we suggest that when there is the need for continuous use of LAIs, paliperidone palmitate is an option with minimal EPS than the FGAs.

Contribution Categories	Name of Author
Follow up of the case	F.O., E.Y.
Literature review	E.Y., B.O.Y.
Manuscript writing	E.Y., F.O., B.O.Y.
Manuscript review and revision	E.Y., F.O., B.O.Y.

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