

CASE REPORT

A CASE OF TARDIVE DYSKINESIA WITH PALIPERIDONE PALMITATE

Philip Kumar Boyanapally¹, Nishanth Vemana², Phani Prasant Mulakaluri³

Senior Resident^{1,2}, Consultant Psychiatrist³, Chetana Hospital, Secunderabad, Telangana

ABSTRACT

Background: Tardive dyskinesia is a neurological side effect of long term antipsychotics use. Incidence is common and found to be less prevalent with second generation antipsychotics than the first generation antipsychotics.

Case Description: We present to you a case of Tardive Dyskinesia in a 45 year old female after 18 months use of injection Paliperidone Palmitate.

Discussion: Incidence of Tardive dyskinesia has been reported to be low with both oral and injectable paliperidone, but no cases are reported in India.

Conclusion: This case is a stark reminder that all antipsychotics on prolonged use can cause TD and the clinician should be vigilant to recognise and address this debilitating symptom even with the new generation antipsychotics.

Keywords: Paliperidone Palmitate, Long Acting Injectable Antipsychotic, Tardive Dyskinesia

INTRODUCTION

Tardive dyskinesia (TD) is generally a late occurring and sometimes persistent complication of long term treatment with anti-psychotic drugs. The term TD was coined by Faurbye and colleagues in 1967.

TD is a hyperkinetic movement disorder characterised by repetitive, involuntary, purposeless movements commonly involving the oral, lingual, buccal area, face, trunk & extremities.^[1,2]

Typical involuntary movements include tongue thrusting, lip smacking, lip pursing, grimacing, chewing movements, rocking of trunk, pelvic thrusting, marching in place, irregular respiration and repetitive sounds such as humming or grunting.

The prevalence of TD is around 20-50% of all patients treated with neuroleptics and the prevalence increases with increasing age. TD is a clinical diagnosis and before the diagnosis is made the clinician should exclude other causes of movement disorders. Around 14% of drug naïve schizophrenia patients have involuntary movements and 1-8% of older adults develop spontaneous oral facial dyskinesias (senile dyskinesia).^[3]

To meet the criteria of TD, the symptoms must develop after at least 3 months of exposure to dopamine antagonist (or 1 month in patients with age 60 or more)

Address for correspondence:

Dr Phani Prasant Mulakaluri

Consultant Psychiatrist

Chetana Hospital, Secunderabad, Telanagana. 500003

Email: drphani@gmail.com

Ph: 9849807740

or within 4 weeks of withdrawal from oral medication (or 8 weeks of withdrawal from depot medication) and should persist for at least 4 weeks after discontinuation of offending drug.^[3]

Pathophysiology of TD is poorly elucidated. The different mechanisms postulated are as follows

- Prolonged blockade of post synaptic dopamine receptor^[1,4]
- Dopaminergic hypersensitivity^[5]
- GABA dysfunction^[6]
- Cholinergic hypo function
- Excitotoxicity

Atypical antipsychotics have generally shown a better safety profile compared with conventional antipsychotics, particularly in terms of a lower risk for TD (0.8% vs 5.4).^[7,9]

Long-acting Injectable (LAI) antipsychotics provide more continuous, effective blood levels than daily oral antipsychotic medications thus, eliminating the need for daily treatment and overcoming a significant barrier to optimal medication management for many patients. However, some reports suggest that compared with oral antipsychotics, LAI may increase acute Extra Pyramidal Syndrome (EPS) in patients with schizophrenia^[10], and likely to be a risk factor for TD.^[11] Thus, with the increasing availability and use of LAI atypical antipsychotics, TD associated with LAI formulations may be a concern for clinicians and patients.

Paliperidone (9-hydroxyrisperidone) is an active metabolite of another atypical antipsychotic, risperidone. Paliperidone is a potent inhibitor of the

dopamine D2 receptor; according to the dopamine super sensitivity hypothesis, the blockade of striatal D2 receptors by antipsychotic drugs up-regulates the striatal dopaminergic system and subsequently, may result in TD

CASE HISTORY

Mrs P, a 45 year old married female, studied up to B Sc. and currently a homemaker presented to Chetana Hospital with behavioural disturbances in May 2014. On further clarification there was a family history of schizophrenia and Major depressive disorder in two of her 1st degree relatives. Her medical history is unremarkable. Her illness started in 2007 when she was diagnosed as having Paranoid Schizophrenia for which she underwent treatment. She also had multiple exacerbations in the past mainly due to Non-compliance with the medication. She showed good response to various antipsychotics but would stop it repeatedly due to side effects like sedation, slowness and constipation.

In May 2014 she presented with delusions of persecution, delusions of reference, command hallucinations. A diagnosis of paranoid schizophrenia was made and was started on Olanzapine (20mg). In view of her non-compliance option of depot antipsychotics was discussed with the husband. Paliperidone was chosen due to advantage of monthly once dosing and less EPS propensity. A loading dose strategy was used with 150mg on day 1 followed by 100mg on day 7. A maintenance dose of 100mg was given; oral olanzapine was withdrawn within 3 weeks. She responded within a month and her positive symptoms came down.

In the follow up, she complained of weakness, slowness, lethargy and a motivation. Paliperidone dose was reduced to 75mg, Trihexyphenidyl(2mg) was added in view of propensity to EPS and diazepam(5mg) was added to alleviate sleep disturbances. In spite of dose reduction and adding trihexyphenidyl the above mentioned symptoms persisted, when they were considered as negative symptoms and low dose Amisulpride (50-200mg) was started. There was no improvement and it was discontinued after 4 weeks. Escitalopram 10mg was tried but it was discontinued as she could not tolerate it.

From March 2015 she was only on Paliperidone 75mg/month, Trihexyphenidyl 2mg and Diazepam 5mg. This dose continued till September 2015 when she developed lingual and perioral dyskinetic movements. On Abnormal Involuntary Movement Scale (AIMS) she scored 3 in two areas (lingual and perioral) which showed a POSITIVE AIMS examination. Paliperidone was stopped completely and oral olanzapine was

restarted. By November 2015 lingual and perioral movements have become much lesser with decrease in distress. AIMS score was 1 in both areas which indicate a NEGATIVE AIMS examination.

Her symptoms were under control with Olanzapine 20mg and she is currently in remission.

DISCUSSION

TD is a chronic disabling condition with marked distress to the patient. It affects the quality of life of the individual. SGA LA Injectable is promoted as being less prone to such side effects.

In the European schizophrenia outpatient health outcomes study (SOHO) 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.^[11] Paliperidone ER has shown more potent occupancy at the dopamine D2 receptor than risperidone.^[12] There is evidence in the literature about incidence of TD with Paliperidone.

In a recent posthoc analysis studying the incidence of TD in Paliperidone oral vs Long Acting Injectable (LAI) showed that incidence of TD with Paliperidone is very low irrespective of the formulation used (<0.2%), incidence of TD in LAI Paliperidone was around 0.12% which is much lesser compared to First Generation depots.^[13] They also reported that incidence of TD was high in the first month of the treatment and steadily decreased over time.

This case is significant for occurrence of TD after 1.5 years of receiving Paliperidone Palmitate Long Acting Injectable. During the last 6 months it was the only antipsychotic (75mg) used in this patient along with Trihexyphenidyl (2mg) and diazepam(5mg). In our case risk factors for development of TD were female sex, long duration of illness & exposure to antipsychotics, prolonged use of anticholinergic agent and intermittent drug treatment. The intensity of dyskinetic movements reduced on discontinuation of Paliperidone. To our knowledge there are no published reports of TD with injectable forms of Paliperidone from India.

This case is a stark reminder that all antipsychotics on prolonged use can cause TD and the clinician should be vigilant to recognise and address this debilitating symptom.

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