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Letter to Editor

Management of tardive syndromes with clozapine: A case series

A B S T R A C T

Tardive syndromes are among the most debilitating side effects associated with use of antipsychotics. In this case series we present 5 cases of drug induced tardive syndromes, who had not responded to many of the other therapeutic measures but responded to clozapine. The response rate with clozapine varied from 50% to 100% and the response was seen by week 3 in most cases. Over the long term follow-up of as long as 6 years the response to clozapine was sustained. In two cases clozapine could be stopped.

Keywords:
Clozapine
Tardive syndromes
Tardive dystonia
Tardive dyskinesia

Tardive syndromes (TS) are delayed onset disorders associated with use of dopamine receptor blocking agents and are classified as tardive dyskinesia, tardive dystonia, tardive akathisia, tardive stereotypy, tardive tourettism, tardive myoclonus, tardive tremor and tardive Parkinsonism (Fernandez and Friedman, 2003; Bhidayasiri and Boonyawairoj, 2011).

Clozapine has been shown to improve TS in some cases and some reports suggest worsening/development of tardive syndromes with clozapine (Hazari et al., 2013). However, most of the data about usefulness of clozapine in TS is limited to patients with psychotic illnesses and there is limited data about usefulness of clozapine in management of TS in patients with affective disorders. In view of the limited literatures, in this report we present 5 cases (4 with affective disorder and one with delusional disorder), who presented with antipsychotic induced TS (dystonias and dyskinesias) and were treated with clozapine for their TS. While on clozapine these patients were monitored regularly for blood counts.

Case 1: Ms P, a 49 year was diagnosed with anxious avoidant personality, recurrent depressive disorder (RDD), hypothyroidism and hypertension. She developed involuntary grinding movement of the jaw and sudden protrusion of tongue along with cervical dystonia about 2 years back following exposure to amisulpiride (50 mg/day) for 5 months. Additionally she was treated with other psychotropics (see Table 1) along with eltroxine and antihypertensives. Over the period her symptoms worsened and she had relapse of her Major Depressive Disorder [Hamilton depression rating scale (HDRS) score-30]. Detailed workup did not reveal any organic cause for her movement disorder. She was treated with venlafaxine, clonazepam and clozapine (see Table 1). With this treatment her depression remitted and the movements reduced significantly over the period of 6 weeks. Over the period of next 3 months all her dyskinetic and dystonic movements subsided. After 2 years of therapy dose of clozapine was reduced from 150 mg/day to 100 mg/day without any worsening of the movement disorders and was eventually stopped without any worsening of TS.

Case 2: Ms. M, a 40 year, presented with a history of bipolar affective disorder of 25 years. About 7 months prior to coming in contact with us, for one of her relapses, she was treated with risperidone 5 mg/day with which she developed involuntary repetitive, non rhythmic stereotyped movements involving the lingual and oral region in the form of grimacing, puckering, smacking and pouting movements. The movements kept on worsening and involved upper facial regions in the form of blinking of eyelids, frequent frowning and wrinkling of forehead. Later she developed twisting movements of the neck lasting 30–60 min. When seen at our clinic she was euthymic. She was started on clozapine, with which she showed improvement in her symptoms of movement disorder by 70% within 6 weeks of starting of treatment with clozapine (Table 1).

Case 3: Mr. M, 54 year was suffering from persistent delusional disorder for last 30 years and diabetes and hypertension for 5 years. He developed tardive movements while receiving risperidone. The movements were characterised by orofacial dyskinesia, blepharospasm, cervical dystonia, chorieform movements of bilateral upper limbs and lower limbs. He was more or less bed bound as he was not able to communicate and see because of his movement disorder. When first seen by us his delusional disorder was in remission. After proper evaluation and ruling out the organic causes, he was started on clozapine (see Table 1) along with clonazepam. Over the period of initial 8 weeks he achieved about 50% improvement in his movement disorder and over the next one year there was further reduction in the movement with overall improvement of 60–70%. He maintained the same level of improvement up to 6 years follow up.

Case 4: Ms. U, 29 year, diagnosed with RDD, developed tardive dystonia 9 months prior to presenting to us while receiving amisulpiride. Dystonias lead to abnormal posturing of the neck and lumbar region which led to broad based gait while walking. At the time of presentation she had moderate depression (HDRS score 18). Patient was started on clozapine, with which she showed improvement in dystonia over the period of 2 months (Details of medication given in Table 1). She followed up for the period of 2 years while on clozapine without any recurrence of movement disorders, after which clozapine was stopped and she maintained well over the next 1 year.

Case 5: Mr. S, a 52 year, diagnosed with mixed anxiety and depressive disorder developed Meige's syndrome (blepharospasm

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Table 1
Details of patients treated with clozapine for TS.

Age/Sex	Antipsychotic use prior to development of tardive syndrome	Other drug use (in mg/day) prior to development of tardive syndrome	Type of movement disorder	Drugs used for management of tardive syndromes and psychiatric morbidity before clozapine	Clozapine dose in mg/day	Other drugs for management of Tardive syndrome	Abnormal Involuntary Movement Scale (AIMS) score prior to starting clozapine	Other medications used for management of psychiatric disorder	Duration of clozapine	Outcome
P 49/F	Amisulpride 50 mg 5 months Levosulpride 100 mg 3 months	Escitalopram 20 mg–40 mg Paroxetine 12.5 mg Propranolol 10 mg	Tardive dyskinesia involving eyelids, orofacial, lingual, along with cervical dystonia and drug induced Parkinsonism	Olanzapine 10 mg Diazepam 10 mg Clonazepam 5 mg Baclofen 30 mg Tetrabenazine 50 mg Trihexyphenidyl 6 mg Botulinum toxin Levodopa/ carbidopa 100/10 mg (for Parkinsonism)	150	Clonazepam 0.5–3 mg for initial 4 weeks	23	Venlafaxine 225 mg/day	2.5 years	AIMS – 6 (75% reduction) at 8 weeks 60% subjective improvement by 8weeks. Onset of improvement noticed by day 18. Complete improvement by 18 weeks. Improvement sustained at 2.5 years follow up after stopping clozapine.
M 40/F	Past details not available Risperidone 5 mg 2 weeks Trifluperazine 15 mg (after start of dyskinesia)	Lithium 900 mg Fluoxetine 40 mg Carbamezapine 600 mg	Tardive dystonia involving cervical region and tardive dyskinesia involving eyelids, perioral and lingual areas	Trihexyphenidyl 6 mg Diazepam 15 mg Clonazepam 3 mg Promethazine 75 mg Carbamezapine (for BPAD)	62.5	Clonazepam 1.5 mg for initial 4 weeks	25	Nil	8 weeks	AIMS – 15 (40% reduction) 60% subjective improvement Onset of improvement noticed by week 3.
Mr. M 54/M	Past details not available- intermittently several years Risperidone 6 mg 1 year	Nil	Tardive dystonia involving cervical region, respiratory and pharyngeal muscles + tardive dyskinesia involving eyelids, orofacial region, upper limbs, lower limbs	Olanzapine 5 mg Tetrabenazine 215 mg Baclofen 80 mg Clonazepam 6 mg Lorazepam 2 mg Trihexyphenidyl 10 mg Levodopa/ carbidopa 200/20 Promethazine Eszopiclone Botulinum toxin	175	Clonazepam 6 mg Vit E 500 mg continued along with clozapine	31	Nil	6 years	AIMS – 13(58% reduction) 70% improvement as per subjective reporting, Onset of improvement noticed by day 10 Improvement sustained for 6 years with continuation of clozapine.