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A Study on Drug-Induced Tardive Dyskinesia: Orofacial Musculature Involvement and Patient's Awareness

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Abstract

Objective: Schizophrenia is a psychiatric disorder that requires long-term treatment. Long-term antipsychotic treatment is often associated with the emergence of tardive dyskinesia (TD), the severity of which is measured by Abnormal Involuntary Movement Scale (AIMS). This study examined the relationship among TD, orofacial musculature activity, and patient's awareness of AIM. The knowledge would help dentists to deliver oral care for schizophrenics with TD.

Materials and Methods: We identified 317 patients from a standard, data sharing initiative, of whom 38.3% exhibited AIM score of 2 to 15. The patient demographics, drug history, details of AIMS were subjected to descriptive and inferential statistical analysis using SPSS with $P \leq 0.05$ as significance.

Results: The mean of only orofacial features ($n = 56$) was 3.43 ± 2.68. Muscles of facial expression was involved in nine (7.9% of all TD), lip/perioral area in 27 (23.68%), jaw in 52 (45.61%), and tongue in 77 (67.54%). The patient's perception of AIM precipitated stress when involving jaw, tongue, limbs, and trunk was statistically significant ($P \leq 0.05$). The multiple regression model statistically significantly predicted TD for factors considered.

Conclusion: Around 1% of global population is being diagnosed with schizophrenia, carry an inherent risk of developing TD. They might have orodental care requirements, including

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Conflicts of interest

There are no conflicts of interest.

prosthodontic and restorative services. Primary physicians and dentists need to be aware of TD and its mechanism for appropriate patient management.

Keywords

Antipsychotics; *movement disorders*; *oral abnormal movements*; *oral health care*; *schizophrenia*; *tardive dyskinesia*

Introduction

Oral health and mental health are integral parts of general health. There has been recent call for considering a multidisciplinary, multiorgan inclusive consideration for proper oral health.[1] The mental disorders and consequent drug therapies carry an inherent risk for orofacial-dental disorders.[2] One of these side effects is least studied in literature is tardive dyskinesia (TD). It is a nongoal- related, repetitive, involuntary movement disorder that is often attributed to prolonged neuroleptic and other similar drug intake. It was first described as an entity in 1959 by Sigwald with cephalic involvement, which they referred as "facio-bucco-linguo-masticatory dyskinesia," later renamed as "bucco-linguo- masticatory (BLM) syndrome" and modified as "tardive dyskinesia" by Uhrbrand and Faurbye in 1960.[3–7] By definition, TD is initiated and progresses after administration (usually long-term, but reported with short term) of neuroleptic such as phenothiazines, butyrophenones, and thioxanthenes.[4] These drugs may interfere with dopamine transmission in the brain.

The exact mechanism of TD has not been elucidated. There are several hypothesis proposed. It includes D2 receptor upregulation with subsequent hypersensitivity, GABA insufficiency, increased opioids (encephalin and dynorphin), glutamate and excitotoxicity, oxidative stress and cell injury, and genetic susceptibility. It has also been shown that typical antipsychotics tightly bind and would remain attached to D2 receptors for a longer time (a few days) than newer "atypical" agents (12–24 h). Thus, typical antipsychotics produces the more antipsychotic effect as well as higher tendency to produce TD.[8–17] In a large- scale meta-analysis involving 34,555, patients in between 1959 and 1979 showed the prevalence of TD between 20% and 50% of all patients on neuroleptics.[18] Recent analysis of studies published during 2000 to 2015 involving 11,493 patients identified, a global TD prevalence of 25.3% among antipsychotic drugs users.[9,17,19–21]

A most common manifestation of TD is orofacial chorea, akin to the spontaneous variety and involves 80% of TD. The craniocervical region, often the "BLM triad" is most commonly involved. It includes repetitive and stereotypic oral movements including but not limiting to facial grimacing, tongue protrusion, puckering, smacking/licking of lips, side-to-side jaw motion, involuntary jaw opening, twisting, curling or protrusion of the tongue, chewing or lateral jaw movements, pursing, sucking, pouting, or puckering of the lips, facial tics, frequent eye blinking, and even dysphagia. Most of the oral TD does not cause a *de novo* pain or disabilities but can pose severe sociological impairment/isolation, distress, embarrassment, anxiety, depression, and even stigmatization. The movements may precipitate oral problems, including oral ulceration, speech impairment, decreased salivation (due to other side effects of the drugs), and may aggravate issues especially with dentures

and implant placement[4–6,15,16] As the oral/perioral region are commonly involved, the patient may present to dentists for management as well as dentist may face problem while rehabilitating TD patients. In addition, as the movements in oral tissues can be well-observed, deep knowledge of etiopathogenesis and TD presentation in oral region, could help the psychiatrist for early diagnosis and management of TD.

Reports of TD are less common in neurological and psychiatric literature, and there is a paucity of reports on TD in general literature, especially the extent of oral manifestation and awareness patterns.[4,5] The present manuscript aims to describe in detail the orofacial characteristics of TD with a stress on self-awareness.

Materials and Methods

As reported earlier, the prospective and retrospective methods used to study TD have inherent issues.[12,22] Data used in this manuscript were obtained from the SchizConnect database (http://schizconnect.org), Collaborative Informatics and Neuroimaging Suite Data Exchange tool (http://coins.mrn.org/dx), and Mind Research Network.[23,24] The investigators within SchizConnect or those who contributed to the design and implementation of SchizConnect and/or provided data but did not participate in analysis or writing of this report. All data were downloaded as .CSV format, entered, and analyzed using Statistical Package for Social Services (SPSS, Version 23; IBM, Armonk, New York, USA). Descriptive statistics and inferential statistics were performed as outlined below. $P \leq 0.05$ was taken as significant.

Baseline data of patients in SchizConnect database, who had the Abnormal Involuntary Movement Scale (AIMS)[25,26] recorded, were only included in this study. AIMS is a universally accepted, validated questionnaire that documents the AIM on a 5-point questionnaire with 12 questions. It contains four questions on orofacial movements, three on extremities-trunk movements, three on global judgment, and last two relates to dental status. Only data of those with demographic details of gender, AIM score, and disease status were considered for this study.

As we intended to study the influence of TD on dental status, we employed only the first 10 questions, eliminating the dental status to arrive at the AIM score (≥2). From this, the AIM score, TD (presence/absence), orofacial AIM, and limb-trunk AIM scores were computed. Details of the disease, age, gender, the auto-calculated sum of all olanzapine equivalent doses taken by the participant, the auto-calculated sum of all chloropromazine equivalent doses taken by the patient were acquired. The features were compared against the perception of patient's awareness of AIM. The TD status was compared with demographic parameters and AIMS. The subscales of orofacial and limb-trunk AIM scores was then used to classify the patients to have orofacial AIM, limb-trunk AIM, both together or no AIM. The parameters were compared using appropriate statistics. To identify the relationship, AIMS parameters was assessed for correlation with TD, AIM (muscles of facial expression, lips and perioral area, jaw, tongue), severity of AIM, incapacitation due to AIM, patient's awareness of AIM, AIM score, and TD. To identify the most important factor that contributes to AIM score, regression test was performed.

Result

The search yielded 317 patients from two studies, of whom most of the relevant data were available for 298 patients. The study group were on antipsychotic medications for schizophrenia (Strict, $n = 161$), (Broad, $n = 89$), schizoaffective ($n = 38$), and bipolar disorder ($n = 10$). The AIM score was 0 in 160 (53.5%) and 1 in 24 (8.11%) patients. The rest 38.3% had a score ranging from 2 to 15 with a mean of 5.82± 3.56 and a median of 5. Only 114 (38.3%) had TD. The mean range of only orofacial features (for four parameters, $n = 56$) was 3.43 ±2.68 (1–12), only limb-trunk features (three parameter, $n = 21$) was 3.48 ±2.91 (1–11), whereas for combined ($n = 57$), it was 7.33 ±3.69 (2–15). Muscles of facial expression was involved in nine (7.9% of all TD), lip/perioral area in 27 (23.68%), jaw in 52 (45.61%), and tongue in 77 (67.54%).

Table 1 shows the difference between demographic, clinical features and drug characteristics between TD and non-TD. Denture wearing and sum of equivalent olanzapine and chlorpromazine were not significant, whereas others were statistically significant. The patient' s perception of AIM precipitated stress when involving jaw, tongue, limbs, and trunk was statistically significant, whereas sex, disease, muscles of facial expression, and lip/perioral area movements were not significant [Table 2].

The data indicated that patients have been either on a mono/ multidrug therapy and drugs were often changed in visits. As this part of the data was obscure, the type of drugs, duration, and frequency were not included for this study. The sum of total equivalent doses of chlorpromazine and olanzapine was not statistically significant between grades of TD in all demographic parameters and contributing factors, except for olanzapine in lip/perioral musculature, were it was significant ($P = 0.029$).

It was observed that the non-TD group had relatively young age as compared to TD group, when all parameters were compared [Tables 1 and 3]. Correlation of AIM score, TD, and various oral abnormal movements was performed using correlation statistics. The muscles did not correlate much with each other, whereas other parameters were correlated significantly [Table 4].

Table 5 shows the difference among only orofacial AIM, only limb/trunk AIM, combined AIM in terms of other parameters. Among non-TD ($n = 184$), 12 (6.52%) cases had only orofacial movements, and eight (4.35%) cases had limb movements. In TD, there was exclusive orofacial ($n = 44$, 38.6%), limb-trunk ($n = 13$, 11.4%), and combined ($n = 57$, 50%) pattern. All parameters exhibit a distinct pattern between the four subcategories. However, denture wearing was not statistically significant [Table 5].

Logistic regression test were performed with clinical parameters for AIM scores. There was linearity as assessed by partial regression plots and a plot of studentized residuals against the predicted values. There was independence of residuals, as assessed by a Durbin-Watson statistic of 1.958. There was homoscedasticity, as assessed by visual inspection of a plot of studentized residuals versus unstandardized predicted values. There was no evidence of multicollinearity, as assessed by tolerance values greater than 0.1. There were no studentized deleted residuals ≥±3 standard deviations, no leverage values ≥0.2, and values for Cook's

distance > 1. The assumption of normality was met, as assessed by a *Q-Q* plot. The multiple regression model statistically significantly predicted survival, $F(14, 283) = 248.77$, $P < 0.0005$, adjusted $R^2 = 0.93$. All variables added statistically significantly to the prediction, $P \leq 0.05$. Regression coefficients and standard errors can be found in Table 6.

Discussion

Drugs for psychiatric disorders causes a specific pattern of orodental diseases. Uncoordinated muscle movement disorders are a part of this spectrum and has been increasingly reported.[4–6] In normal individuals, movements are planned at the prefrontal cortex and the information passed on to the premotor cortex, supplementary motor area, and then to the primary motor cortex. The upper motor neurons which control the facial and oral movements are situated near the Sylvian fissure and axons converge and descend in the cerebral peduncle to the midbrain forming corticobulbar tract or spinal cord corticospinal tract. The neurons synapse with motor nuclei of cranial nerves to serve the orofacial musculatures. The extrapyramidal network system (EPS) is a network of neural fibers associated with coordination of movement and forms a part of the motor system. The EPS arise from pons, medulla, and are modulated by various part of CNS, including striatum and basal ganglia (BG) with dopamine being the main neurotransmitter. The function of EPS includes control of muscle tone, body posture, harmonize motor activity, and modulate functions such as the finer aspects of voluntary and involuntary movements.[6]

The BG regulates the initiation, grading, and control of the amplitude and direction of movement. It modulates to create fine and coordinated movements. When there is biochemical or structural abnormalities in this modulation mechanism, the BG loses its control causing unwanted motor activity.[6,12,27]

Movements are also modulated in the EPS *via* a “direct” or “indirect” pathway. The direct pathway projects from motor striatum to globus pallidus interna (GPI) and facilitates “go” signal. The indirect pathway projects in to the GPI *via* globus pallidus externa and subthalamic nucleus to mediate “stop” signals. Dopamine at D1 receptors in direct pathway interact with NMDA receptors, whereas the D2 receptors in indirect pathway inhibit “stop” signals, thereby causing “more go.”[12]

In schizophrenic brain, there appears to be too much of dopamine release. The chronic D2 receptor blockade via the antipsychotic drugs, in the motor striatum causing upregulation of supersensitive D2 receptors, often in motor striatum, causing “more go” signals, causing abnormal, hyperkinetic movements. In addition, different parts of the brain react differentially to chronic D2 blockade contributing mixed or variation in signals.[12] The mechanism of TD is not completely elucidated, and there has been no plausible explanation why orofacial musculature, particularly tongue is more commonly affected than other parts of the body.

The orofacial component has been described as the most common sign of TD. There is a paucity of general literature with respect to the extent of the orofacial musculature involvement, self-perception, awareness, and differences in detail between non-TD and TD.

[4–6] This manuscript aimed to address the lacunae so as to design prospective studies to understand the mechanism of TD development. In this complete random sample of patients on antipsychotics, the TD prevalence of 38.26% was observed. Twenty more cases had milder symptoms that could not be called as TD as per definition. Among non-TD (n = 184), 12 (6.52%) cases had only orofacial movements, and eight (4.35%) cases had limb movements. In TD, there was exclusive orofacial (n = 44, 38.6%), limb-trunk (n = 13, 11.4%), and combined (n = 57, 50%) pattern. In all, 113 patients (37.92%) had at least one feature suggestive of orofacial TD, whereas only 78 patients (26.17%) had features of limb-trunk TD. This trend clearly indicates that orofacial AIM occurs most commonly in TD. Among orofacial musculatures, tongue is the most commonly involved site, particularly even when positioned at rest. Instruments to measure the tongue forces in TD have been built to identify even early TD so as to initiate treatment.[28,29] This trend has been previously reported by TD reports from China.[17] Identification of the offending drug and concentration is vital for management of orofacial TD. Removal of the offending drug is the primary approach, whereas motor suppressive medications may be another therapeutic options that needs to be undertaken with caution.[4] Dental treatment of TD patients is challenging. Protection to tongue and other vital oral structures is to be taken before commencing treatment. Every care needs to be taken to ensure that instruments do not harm the TD patients.

The TD and non-TD presentations differ distinctly with age. The non-TD has a distinctly lower age than the TD group. This was consistent with previous reports.[10,13,18,19] In addition, the drug dose/total dose-equivalents of drugs were also significant across the TD/non-TD groups. This indicates that the duration of the use of drug could be a major factor that determines the TD outcome. The difference in age is in support of this fact. As the data availability for length of drug use was limited, no valuable information could be further elicited. In the regression model, the adjusted R^2 of 0.93 indicates that the model could explain only up to 93% of the factors considered. The other factors such as type of antipsychotics (typical/atypical), duration of use, or frequency of use may contribute to the remaining 7%. Further studies have to confirm the role of these factors. These results are in line with the previous reports of TD from Chinese patients.[17]

There is a difference in correlation pattern between AIM score to that of orofacial musculatures. With respect to the muscles of mastication, AIM was only related significantly to lips/perioral musculature, whereas the lips/perioral musculature related significantly to all orofacial muscles. Jaw and tongue musculature AIM were not statistically significant with muscles of mastication TD. Patient's awareness of AIM did not correlate significantly with muscles of mastication AIM. This indicates that the different parts of the orofacial musculatures react differently to the TD pathogenesis. Tongue appears to be the frequently involved orofacial musculature, whereas muscles of facial expression the least. Involvement of tongue poses additional issues such as frequent trauma to tongue, stability issues posed, whereas treating with removable dentures and even may pose a significant problem while treating them.[30] There has been several case reports in this regard and even an attempt to diagnose early TD with help of the tongue force.[4–7,29,30]

Among the orofacial musculature involvement, the jaw and tongue movements only caused varying level of distress, but this did not carry any statistical significant difference in the muscles of facial expression and lip/perioral musculature AIM. The regression statistics reveal that a significant number of patients with AIM score (≥2) have denture or tooth-related issues with a standardized coefficients $\beta = 0.037$ and unstandardized coefficient $\beta = -0.397$, $P = 0.044$. This indicates that a significant number of the study population with AIM have orodental problems. This subset of patients needs dentist attention, and this fact also underlines the need for the dentist, to understand more about TD in detail. In addition, it has been shown that the cognition deficits is relatively higher among those schizophrenics that are affected by orofacial TD.[3,31]

Study limitations

The study has inherent methodological limitations of the secondary data analysis of TD.[12] Cutoff values of AIM score are often varied which can lead to varied independent conclusions.[17,25,26] The frequency of movement, muscle tone/ feedback, and so on have not be accounted in the database, in future should be considered. Intra and interobserver variability of scoring, reliability of AIM scores are also some factors that need to be taken in to consideration. Studies with large samples and followed longitudinally needs to be undertaken to verify the findings of the present study.

Clinical translation

Quality of life in schizophrenic patients are varied, depending on the progression of the condition and often linked to their disease status and medications.[32] The medication side effects are measured by various scales, and AIMS is a widely used scale for measuring movement disorder.[26] With oral involvement being much early and common in TD, an alert and informed psychiatrist would diagnose/manage TD better. Hence, there is a need for the present study.

About 1% of global population are being diagnosed with schizophrenia and are treated, often with typical and atypical antipsychotics.[33] With the longevity of life increasing, the number of patients on these drugs living with increased life span are bound to increase. In addition, with prolonged use of drugs, especially atypical first-generation neuroleptics for economic reasons, occurrence of TD is bound to increase. Increased geriatric population with/without psychiatric drug prescription may present to dentists or primary care physicians for treatment. They would need more knowledge to provide medical guidance to TD patients. Examination of orofacial aspects of TD would yield valuable clues about the initiation of extrapyramidal syndrome in these patients that would help to identify, monitor, intervene, or successfully manage the condition, increasing the quality of life in these patients.

Conclusion

TD is a common, understudied side effect of first-generation neuroleptics, which are commonly prescribed in developing and underdeveloping countries. Tongue is the major orofacial muscle to be involved in TD, which the patient perceives and is stressed due to this

disorder. Duration of drug use and age was crucial factors that determine TD, whereas dose of drug/ drug equivalence is not. TD patients often have dental issues, and most of them are in need of dental treatments. Knowledge of orofacial TD are important for primary care physicians and psychiatrist to identify the initial manifestation to understand, identify, and treat the same at presentation of early signs and symptoms.

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References

1. Cohen LK, Dahlen G, Escobar A, Fejerskov O, Johnson NW, Manji F. Why a radical overhaul of dentistry is needed. Indian J Dent Res 2017;28:471–4. [PubMed: 29072204]
2. Fratto G, Manzon L. Use of psychotrophic drugs and associated dental diseases. Int J Psychiatry Med 2014;48:185–97. [PubMed: 25492713]
3. Merrill RM, Lyon JL, Matiaco PM. Tardive and spontaneous dyskinesia incidence in the general population. BMC Psychiatry 2013;13:152. [PubMed: 23714238]
4. Clark GT, Ram S. Orofacial movement disorders. Oral Maxillofac Surg Clin North Am 2016;28:397–407. [PubMed: 27475514]
5. Clark GT, Ram S. Four oral motor disorders: Bruxism, dystonia, dyskinesia and drug-induced dystonic extrapyramidal reactions. Dent Clin North Am 2007;51:225–43. [PubMed: 17185068]
6. Heir GM, de la Hoz JL. Orofacial dystonias and dyskinesias In: Ferreira JNAR, Fricton RhodusN J, Eds. Orofacial disorders. 1sted Switzerland: Springer International Publishing; 2017 pp. 171–88.
7. Kleopa KA, Kyriakides T. A novel movement disorder of the lower lip. Mov Disord 2004;19:663–704. [PubMed: 15197704]
8. Waln O, Jankovic J. An update on tardive dyskinesia: From phenomenology to treatment. Tremor Other Hyperkinet Mov (NY) 2013;3 tre-03–161–4138–1.
9. Cornett EM, Novitch M, Kaye AD, Kata V, Kaye AM. Medication- induced tardive dyskinesia: A review and update. Ochsner J 2017;17:162–74. [PubMed: 28638290]
10. Lerner PP, Miodownik C, Lerner V. Tardive dyskinesia (syndrome): Current concept and modern approaches to its management. Psychiatry Clin Neurosci 2015;69:321–34. [PubMed: 25556809]
11. Moore TJ, Furberg CD. The harms of antipsychotic drugs: Evidence from key studies. Drug Saf 2017;40:3–14. [PubMed: 27864791]
12. Stahl SM. Neuronal traffic signals in tardive dyskinesia: Not enough “stop” in the motor striatum. CNS Spectr 2017;22:427–34. [PubMed: 29205123]
13. Young SL, Taylor M, Lawrie SM. “First do no harm.” A systematic review of the prevalence and management of antipsychotic adverse effects. J Psychopharmacol 2015;29:353–62. [PubMed: 25516373]
14. Strassnig M, Rosenfeld A, Harvey PD. Tardive dyskinesia: Motor system impairments, cognition and everyday functioning. CNS Spectr 2017;1–8. DOI: 10.1017/S1092852917000542.
15. Lees AJ. Odd and unusual movement disorders. J Neurol Neurosurg Psychiatry 2002;72(Supp I):i17–21. [PubMed: 11870199]
16. Donaldson I, Marsden CD, Schneider SA, Bhatia KP. Spontaneous oro-facial chorea and tardive dyskinesia In: Donaldson I, Marsden CD, Schneider SA, Bhatia KP, editors. Marsden’s book of movement disorders. 1st ed New York: Oxford University Press; 2012 pp. 837–53.

17. Hunag Y, Pan L, Teng F, Wang G, Li C, Jin L. A cross-sectional study on the characteristics of tardive dyskinesia in patients with chronic schizophrenia. Shanghai Arch Psychiatry 2017;29: 295–303. [PubMed: 29276353]
18. Kane JM, Smith JM. Tardive dyskinesia: Prevalence and risk factors, 1959 to 1979. Arch Gen Psychiatry 1982;39:473–81. [PubMed: 6121548]
19. D'Abreu A, Akbar U, Friedman JH. Tardive dyskinesia: Epidemiology. J Neurol Sci 2018;389:17–20. [PubMed: 29433811]
20. Stegmayer K, Walther S, van Harten P. Tardive dyskinesia associated with atypical antipsychotics: Prevalence, mechanisms and management strategies. CNS Drugs 2018;32:135–47. [PubMed: 29427000]
21. Salem H, Pigott T, Zhang XY, Zeni CP, Teixeira AL. Antipsychotic-induced tardive dyskinesia: From biological basis to clinical management. Expert Rev Neurother 2017;17:883–94. [PubMed: 28750568]
22. Cloud LJ, Zutshi D, Factor SA. Tardive dyskinesia: Therapeutic options for an increasingly common disorder. Neurotherapeutics 2014;11:166–76. [PubMed: 24310603]
23. Wang L, Alpert KI, Calhoun VD, Cobia DJ, Keator DB, King MD, et al. SchizConnect: Mediating neuroimaging databases on schizophrenia and related disorders for large-scale integration. Neuroimage 2016;124:115–67.
24. Bustillo JR, Jones T, Chen H, Lemke N, Abbott C, Qualls C, et al. Glutamatergic and neuronal dysfunction in gray and white matter: A spectroscopic imaging study in a large schizophrenia sample. Schizophr Bull 2017;43:611–9. [PubMed: 27550776]
25. Rush JA, Jr, First MB, Blacker D, editors. Handbook of psychiatric measures. 2nd ed Washington DC: American Psychiatric Association; 2000 pp. 166–8.
26. van Strien AM, Keijsers JPWC, Derijks HJ, van Marum RJ. Rating scales to measure side effects of antipsychotic medications: A systematic review. J Psychopharmacol 2015;29:857–66. [PubMed: 26156860]
27. Sarro S, Pomarol-Clotet E, Canales-Rodriguez EJ, Salvador R, Gomar JJ, Ortiz-Gil J, et al. Structural brain changes associated with tardive dyskinesia in schizophrenia. Br J Psychiatry 2013;203:51–7. [PubMed: 23222039]
28. Farag AM, Mier RW, Correa LP. Utilizing the concept of geste antagoniste for conservative management of oro-mandibular tardive dyskinesia: A case report and mini-review. Cranio 2016;34:338–42. [PubMed: 26293144]
29. Koning JP, Tenback DE, Kahn RS, van Schelven LJ, van Harten PN. Instrument measurement of lingual force variability reflects tardive tongue dyskinesia. J Med Eng Technol 2010;34:71–7. [PubMed: 19929569]
30. Lumetti S, Ghiacci G, Macaluso GM, Amore M, Galli C, Calciolari E, et al. Tardive dyskinesia, oral parafunction, and implant- supported rehabilitation. Case Rep Dent 2016;7167452 Available at https://www.hindawi.com/journals/crid/2016/7167452/abs/ [PubMed: 28050290]
31. Wu JQ, Chen DC, Xiu MH, Tan YL, Yang FD, Kosten TR, et al. Tardive dyskinesia is associated with greater cognitive impairment in schizophrenia. Prog Neuropsychopharmacol Biol Psychiatry 2013;46:71–7. [PubMed: 23827756]
32. Mohandoss AA. Quality of life in schizophrenic patients: Comparative study from South India. J NTR Univ Health Sci 2017;6:224–31.
33. Charlson FJ, Baxter AJ, Cheng HG, Shidhaye R, Whiteford HA. The burden of mental, neurological, and substance use disorders in China and India: A systematic analysis of community representative epidemiological studies. Lancet 2016;388:376–89. [PubMed: 27209143]

Table 1:

Characteristics of the study population based on tardive dyskinesia and nontardive dyskinesia *

		Non-TD	TD	*P* value
Age	In years	34.64 ± 11.60	42.35 ± 14.16	0.000
Age of initial diagnosis	In years	22.07 ± 8.3	23.61 ±9.58	0.238
Sex	Male	143 (77.7)	92 (80.7)	0.54
	Female	41 (22.3)	22 (19.3)	
Disease	Bipolar disorder	7 (3.8)	3 (2.6)	0.061
	Schizoaffective	30 (16.3)	8(7)	
	Broad schizophrenia	48 (26.1)	41 (36)	
	Strict schizophrenia	99 (61.5)	62 (38.5)	
First degree relative with psychiatric illness	No	88 (83.8)	69 (83.1)	0.527
	Yes	17 (16.2)	14 (16.9)	
Positive and negative symptom scale	Positive scale	15.11 ±4.55	16.38 ±5.03	0.089
	Negative scale	14.96 ±5.52	15.96±5.92	0.262
	General psychology scale	28.93 ± 10.35	29.8 ±8.63	0.561
	Overall scale	58.87 ± 17.79	61.9±15.12	0.249
Muscles of facial expression	Mild	0	7 (2.3)	0.003
	Minimal	3 (1.6)	2 (1.8)	
	None	181 (98.4)	105 (92.1)	
Lip and perioral area	Mild	0	7 (6.1)	0.000
	Minimal	0	16 (14)	
	Moderate	0	4 (3.5)	
	None	184 (100)	87 (76.3)	
Jaw	Mild	0	24 (21.1)	0.0000
	Minimal	3 (1.6)	25 (21.9)	
	Moderate	0	3 (2.6)	
	None	181 (98.4)	62 (54.4)	
Tongue	Mild	0	30 (26.3)	0.0000
	Minimal	6 (3.3)	44 (38.6)	
	Moderate	0	2 (1.8)	

		Non-TD	TD	*P* value
	None	178 (96.7)	37 (32.5)	
	Severe	0	1 (0.9)	
Upper limbs	Mild	0	31 (27.2)	0.0000
	Minimal	7 (3.8)	29 (25.4)	
	Moderate	0	3 (2.6)	
	None	177 (96.2)	51 (44.7)	
Lower limb	Mild	0	18 (15.8)	0.000
	Minimal	1 (0.5)	18 (15.8)	
	None	183 (99.5)	78 (68.4)	
Neck, shoulder, hip	MD	2(1.1)	0	0.005
	Mild	0	2 (1.8)	
	Minimal	0	5 (4.4)	
	None	182 (98.9)	107 (93.9)	
Severity	Mild	0	42 (36.8)	0.000
	Minimal	0	50 (43.9)	
	Moderate	0	5 (4.4)	
	None	184 (100)	17 (14.9)	
Incapacitation	MD	0	1 (0.9)	0.000
	Mild	0	5 (4.4)	
	Minimal	0	11 (9.6)	
	Moderate	0	6 (5.3)	
	None	184 (100)	91 (79.8)	
Awareness	Aware, mild distress	0	10 (8.8)	0.000
	Aware, moderate distress	0	2 (1.8)	
	Aware, no distress	4 (2.2)	32 (28.1)	
	No awareness	180 (97.8)	70 (61.4)	
Current problem with teeth/dentures	No	173 (94)	85 (74.6)	0.000
	Yes	11 (6)	29 (25.4)	
Are dentures usually worn	No	177 (96.2)	102 (89.5)	0.021
	Yes	7 (3.8)	12 (10.5)	
Denture wearing	No	174 (94.6)	107 (93.9)	0.799

	Non-TD	TD	*P* value
Yes	10 (5.4)	7 (6.1)	
The autocalculated sum of all olanzapine equivalent doses taken by the participant	398.48 ±918.21	352.34±371.74	0.923
The autocalculated sum of all CPZ equivalent doses taken by the participant	480.04 ±956.9	429.8 ± 397.45	0.609
Duration of treatment at outpatient setting (months)	81.75 ± 89.52	144.47 ± 149.93	0.015
Duration, living with treatment (in years)	11.85 ± 11.22	19.57±13.38	0.000

[*] ± Indicates standard deviation; value inside brackets “(),” expressed as percentages (%).

Table 2:

Characteristics of study population based on awareness of abnormal involuntary movements*

		Aware, with distress			No awareness	*P* value
		Mild	**Moderate**	**Nil**		
Age of patient (in years)		51.44 ± 8.34	66	40.86 ± 15.01	36.5 ± 12.59	0.000
Treatment duration in OP (months)		160.5 ± 150.97	60	158.46 ± 174.65	96.83 ± 107.06	0.829
Living with disorder for (years)		33 ± 10.96	39	19.21 ± 13.98	13.41 ± 11.64	0.028
Age at initial diagnosis (years)		19.67 ± 5	23 ± 5.66	23.36 ± 9.61	22.82 ± 8.99	0.226
PANSS	Positive	16.38 ± 3.66	10	16.21 ± 4.36	15.58 ± 4.94	0.592
	Negative	19.5 ± 5.63	13	13.44± 3.38	15.54± 5.94	0.06
	GPS	31.5 ± 4.69	22	29.5 ± 7.99	29.2 ± 10.13	0.798
	Overall	67.38± 6	45	58.71 ± 11.87	60.19± 17.78	0.477
Sex	Male	8 (3.2)	0	29 (12.3)	198 (84.3)	0.056
	Female	2 (3.2)	2 (3.2)	7(11.1)	52 (82.5)	
Disease	Bipolar disorder	0	0	3 (30)	7 (70)	0.118
	Schizoaffective	1 (2.6)	1 (2.6)	2 (5.3)	34 (89.5)	
	Broad schizophrenia	4 (4.5)	0	17 (19.1)	68 (76.4)	
	Strict schizophrenia	5 (3.1)	1 (0.6)	14 (8.7)	141 (87.6)	
Muscles of facial expression	Mild	0	0	0	7 (100)	0.406
	Minimal	1 (20)	0	1 (20)	3 (60)	
	None	9 (3.1)	2 (0.7)	35 (12.2)	240 (83.9)	
Lip and perioral area	Mild	1 (14.3)	0	2 (28.6)	4 (57.1)	0.259
	Minimal	2 (12.5)	0	3 (18.8)	11 (68.8)	
	Moderate	0	0	0	4 (100)	
	None	7 (2.6)	2 (0.7)	31 (11.4)	231 (85.2)	
Jaw	Mild	4 (16.7)	2 (8.3)	10 (41.7)	8 (33.3)	0.000
	Minimal	1 (3.6)	0	8 (28.6)	19 (67.9)	
	Moderate	0	0	1 (33.3)	2 (66.7)	
	None	5 (2.1)	0	17 (7)	221 (90.9)	
Tongue	Mild	5 (16.7)	0	14 (46.7)	11 (36.7)	0.0000
	Minimal	1 (2)	0	9 (18)	40 (80)	

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		Aware, with distress			No awareness	*P* value
		Mild	**Moderate**	**Nil**		
	Moderate	0	0	0	2 (100)	
	None	4 (1.9)	2 (0.9)	13 (6)	196 (91.2)	
	Severe	0	0	0	1 (100)	
Upper limbs	Mild	6 (19.4)	0	14 (45.2)	11 (35.5)	0.0000
	Minimal	1 (2.8)	0	7 (19.4)	28 (77.8)	
	Moderate	0	0	1 (33.3)	2 (66.7)	
	None	3 (1.3)	2 (0.9)	14 (6.1)	209 (91.7)	
Lower limb	Mild	3 (16.7)	0	8 (44.4)	7 (38.9)	0.0000
	Minimal	0	0	7 (36.8)	12 (63.2)	
	None	7 (2.7)	2 (0.8)	21 (8)	231 (88.5)	
Neck, shoulder, hip	MD	0	0	0	2 (100)	0.004
	Mild	0	0	1 (50)	1 (50)	
	Minimal	2 (40)	0	0	3 (60)	
	None	8 (2.8)	2 (0.7)	35 (97.2)	244 (84.4)	
Severity	Mild	9 (21.4)	2 (4.8)	17 (40.5)	14 (33.3)	0.0000
	Minimal	1 (2)	0	11 (22)	38 (76)	
	Moderate	0	0	0	5 (100)	
	None	0	0	8 (4)	193 (96)	
Incapacitation	MD	0	0	1 (100)	0	0.000
	Mild	2 (40)	0	1 (20)	2 (40)	
	Minimal	3 (27.3)	0	4 (36.4)	4 (36.4)	
	Moderate	1 (16.7)	0	0	5 (83.3)	
	None	4 (1.5)	2 (0.7)	30 (10.9)	239 (86.9)	

*± Indicates standard deviation; value inside brackets "()," expressed as percentages (%).

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Table 3:

Comparison of mean age (in years ± standard deviation) between tardive dyskinesia patients and nontardive dyskinesia patients based on parameters considered

		Non-TD	TD
Muscles of facial expression	Mild	-	47.29 ± 15.25
	Minimal	24.33 ±2.52	40.5 ± 17.68
	None	34.81± 11.62	42.05 ± 14.13
Lip and perioral area	Mild	-	48.71 ± 16.09
	Minimal	-	45.88 ± 14.9
	Moderate	-	50±5.72
	None	34.64± 11.60	40.8 ± 13.95
Jaw	Mild	-	48.74 ± 14.23
	Minimal	37 ±11.79	40.71 ± 13.98
	Moderate	-	37± 23.64
	None	34.6±11.63	40.87 ±13.40
Tongue	Mild	-	45.13 ± 13.97
	Minimal	37.67± 15.77	38.95 ± 14.59
	Moderate	-	41 ± 19.8
	None	34.53± 11.48	43.94 ± 13.49
	Severe	-	50
Upper limbs	Mild	-	44.81 ± 12.99
	Minimal	34.57±11.312	42.93 ± 14.54
	Moderate	-	54.67 ±4.93
	None	34.64± 11.65	39.69 ± 14.59
Lower limb	Mild	-	31.5 ±4.95
	Minimal	-	51.4±8.56
	None	34.49± 11.58	42.12± 14.31
Neck, shoulder, hip	Mild	-	31.5 ±4.95
	Minimal	-	51.4±8.56
	None	34.49± 42.12	42.12± 14.31
Severity	Mild	-	46.9 ± 14.15

		Non-TD	TD
	Minimal	-	37.73 ± 12.44
	Moderate	-	46.4 ± 12.12
	None	34.64± 11.60	43.47 ± 16.27
Incapacitation	Mild		51 ±4.42
	Minimal	-	47.18 ± 14.78
	Moderate	-	43.67 ±11.93
	None	34.64± 11.60	41.37 ± 14.4
Awareness	Aware, mild distress Aware, moderate distress		51.44 ± 8.39 66
	Aware, no distress	22 ± 2.45	43.22 ± 14.21
	No awareness	34.93± 11.57	40.44 ± 14.17
Current problem with teeth/dentures	No	34.78± 11.60	39.81 ± 13.63
	Yes	32.55± 11.96	49.96±13.15
Are dentures usually worn	No	34.38 ±11.51	41.67 ± 14.42
	Yes	41 ± 13.1	48.55 ± 10.00
Denture wearing	No	34.22± 11.49	41.71 ± 14.19
	Yes	41.8 ± 11.75	53.67 ±7.69

Table 4:

Correlation of abnormal involuntary score, tardive dyskinesia, and oral abnormal movements

		Muscles of facial expression	Lips and perioral area	Jaw	Tongue	Severity of AM overall	Incapacitation due to AM	Patient's awareness of AM	AIMscore	TD
Muscles of facial expression	Correlation	1	0.346*	0.070	0.065	0.223*	0.227*	−0.020	−0.393*	−0.185*
	Sig.		0.000	0.226	0.266	0.000	0.000	0.728	0.000	0.001
Lips and perioral area	Correlation	0.346*	1	0.366*	0.314*	0.381*	0.395*	0.158*	−0.608*	−0.383*
	Sig.	0.000		0.000	0.000	0.000	0.000	0.006	0.000	0.000
Jaw	Correlation	0.070	0.366*	1	0.398*	0.571*	0.139**	0.424*	−0.600*	−0.547*
	Sig.	0.226	0.000		0.000	0.000	0.016	0.000	0.000	0.000
Tongue	Correlation	0.065	0.314*	0.398*	1	0.592*	0.246*	0.374*	−0.668*	−0.674*
	Sig.	0.266	0.000	0.000		0.000	0.000	0.000	0.000	0.000
Severity of AM overall	Correlation	0.223*	0.381*	0.571*	0.592*	1	0.409*	0.569*	−0.791*	−0.846*
	Sig.	0.000	0.000	0.000	0.000		0.000	0.000	0.000	0.000
Incapacitation due to AM	Correlation	0.227*	0.395*	0.139**	0.246*	0.409*	1	0.363*	−0.571*	−0.340*
	Sig.	0.000	0.000	0.016	0.000	0.000		0.000	0.000	0.000
Patient's awareness of AM	Correlation	−0.020	0.158*	0.424*	0.374*	0.569*	0.363*	1	−0.598*	−0.476*
	Sig.	0.728	0.006	0.000	0.000	0.000	0.000		0.000	0.000
AIMscore	Correlation	−0.393*	−0.608*	−0.600*	−0.668*	−0.791*	−0.571*	−0.598*	1	0.782*
	Sig.	0.000	0.000	0.000	0.000	0.000	0.000	0.000		0.000
TD	Correlation	−0.185*	−0.383*	−0.547*	−0.674*	−0.846*	−0.340*	−0.476*	0.782*	1
	Sig.	0.001	0.000	0.000	0.000	0.000	0.000	0.000	0.000	

*Correlation is significant at the 0.01 level (two-tailed).

**Correlation is significant at the 0.05 level (two-tailed).

Table 5:

Difference of abnormal movements based on characteristics studied in the study population[**]

		Abnormal movements				*P* value
		No	**Only orofacial**	**Only limb/trunk**	**Both**	
Severity	Mild	0	16 (28.6)	6 (14.3)	20 (47.6)	0.000
	Minimal	0	25 (44.6)	4 (19)	21 (36.8)	
	Moderate	0	1 (1.8)	0	4 (7)	
	None	164 (100)	14 (25)	11 (5.5)	12 (21.1)	
Incapacitation	MD	0	0	0	1 (1.8)	0.0000
	Mild	0	0	3 (14.3)	2 (3.5)	
	Minimal	0	0	2 (9.5)	9 (15.8)	
	Moderate	0	1 (1.8)	1 (4.8)	4 (7)	
	None	164 (100)	55 (98.2)	15 (71.4)	41 (71.9)	
Awareness of distress	Aware, mild	0	3 (5.4)	3 (14.3)	4 (7)	0.000
	Aware, moderate	0	2 (3.6)	0	0	
	Aware, nil	4 (2.4)	8 (14.3)	5 (23.8)	19 (33.3)	
	No awareness	160 (97.6)	43 (76.8)	13 (61.9)	34 (59.6)	
Current problem with teeth/dentures	No	156 (95.1)	44 (78.6)	16 (76.2)	42 (73.7)	0.000
	Yes	8 (4.9)	12 (21.4)	5 (23.8)	15 (26.3)	
Are dentures usually worn	No	157 (95.7)	53 (94.6)	19 (90.5)	50 (87.7)	0.172
	Yes	7 (4.3)	3 (5.4)	2 (9.5)	7 (12.3)	
Denture wearing	No	156 (95.1)	50 (89.3)	20 (95.2)	55 (96.5)	0.338
	Yes	8 (4.9)	6 (10.7)	1 (4.8)	2 (3.5)	
Mean age		34.56 ± 11.51	38.59 ± 14.81	42.05 ± 12.41	43.53 ± 13.85	0.000
Treatment duration in OP (months)		77.2 ± 83.33	101.21 ± 132.02	207.67 ± 127.55	152.76 ± 158.23	0.001
Living with disorder for (years)		11.39 ± 11.06	18.21 ± 14.59	19.47 ± 7.95	19.68 ± 13.69	0.000
Age at initial diagnosis (years)		22.19 ± 8.4	21.24 ± 7.29	25.87 ± 9.9	24.45 ± 10.75	0.182
Positive scale		15.26 ± 4.61	17.30 ± 5.58	15.93 ± 3.58	15.03 ± 4.74	0.161
Negative scale		15.35 ± 5.56	16.22 ± 5.66	11.93 ± 3.92	16.18 ± 6.27	0.073
General psychopathology scale		29.62 ± 31.15	31.15 ± 10.24	27 ± 5.48	27.97 ± 7.3	0.410
Overall scale		60.14 ± 18.26	64.22 ± 18.31	54.87 ± 10.81	59.18 ± 13.07	0.317

* ± Indicates standard deviation; value inside brackets "(), " expressed as percentages (%).

Table 6:

Coefficients of parameters in logistic regression for AIM score

	Unstandardized coefficients		Standardized coefficients	*t*	Sig.	95% Confidence interval for *B*	
	B	**Std. error**	**Beta**			**Lower bound**	**Upper bound**
Constant	29.253	1.134		25.793	0.000	27.020	31.485
Muscles of facial expression	−2.361	0.186	−0.218	−12.718	0.000	−2.727	−1.996
Lips and perioral area	−0.969	0.109	−0.174	−8.919	0.000	−1.183	−0.755
Jaw	−0.384	0.054	−0.145	−7.087	0.000	−0.490	−0.277
Tongue	−0.590	0.068	−0.181	−8.715	0.000	−0.723	−0.457
Severity of AIM overall	−0.649	0.075	−0.214	−8.636	0.000	−0.797	−0.501
Incapacitation due to AIM	−0.663	0.121	−0.111	−5.494	0.000	−0.901	−0.425
Patient’s awareness of AIM	−0.416	0.055	−0.155	−7.589	0.000	−0.524	−0.308
Current problems with teeth and/or dentures	0.386	0.191	0.037	2.026	0.044	0.011	0.761
Are dentures usually worn?	−0.397	0.266	−0.027	−1.494	0.136	−0.920	0.126
Denture wearing?	0.327	0.281	0.021	1.166	0.245	−0.225	0.880
Upper (arms, wrists, hands, fingers)	−0.413	0.050	−0.172	−8.274	0.000	−0.511	−0.315
Lower (legs, knees, ankles, toes)	−0.989	0.126	−0.146	−7.840	0.000	−1.237	−0.741
Neck, shoulders, hips	−0.335	0.176	−0.030	−1.908	0.057	−0.680	0.011