A STUDY OF ANTIPSYCHOTIC INDUCED TARDIVE DYSKINESIA IN INDIAN POPULATION

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ABSTRACT

Objective: This study was aimed at, to assess the point prevalence and risk factors in Indian population.

Design: Cross sectional comparative study.

Place and duration of study: The sample population was chosen from patients attending Psychiatry OPD of GTB Hospital during two months of the study (October 2004 to November, 2004).

Subjects and Methods: 62 subjects with history of exposure to antipsychotic drugs were included in this study. Their demographic data, illness related factors, and drug history were assessed. Tardive Dyskinesia (TD) was diagnosed according to DSM-IV-TR criteria. Significance of categorical variables was assessed by Chi-Square test and independent t-test was applied for comparison of numerical variables. Odds ratio was calculated using logistic regression.

Results: Point prevalence of TD in this sample was 16%. Advancing age in female gender predicted development of TD. Other known risk factors did not show any statistical significant effect.

Conclusion: Elderly females are at increased risk for development of TD. Point prevalence rate of 16% in mixed sample is fairly high and underscores the need for further studies in this area.

Key words: Tardive Dyskinesia, Neuroleptics, Risk factors.

INTRODUCTION

Tardive dyskinesias (TD) are involuntary movements that usually after long-term neuroleptic therapy. These movements commonly involve orofacial musculature, and appear as puckering, lip-smacking, repeated tongue protrusion, pouting, chewing, facial grimacing etc[1].

Prevalence of TD has been described ranging from 3% to 70% depending upon the sample chosen[1] and the length of exposure to the drugs or higher cumulative doses[2]. Besides neuroleptic exposure there are some other factors that increase the chances of TD if they co-occur in the subjects exposed to antipsychotics. These are older age, female sex, ethnicity (lower chances in Asians than Americans), family history of mood disorders, use of neuroleptic in mood disorders patients, brain damage, substance use, and diabetes[1].

Moreover, presence of TD may impair social relationships, dental problems, weight loss, ambulatory difficulties, speech difficulty[1], therefore it is mandatory to take the informed consent from the patient before exposing him to neuroleptic treatment.

Despite being such a sensitive issue, Indian literature on this subject is scarce and only few reports are available and western data that we use at present to address this issue have ethnic/ genetic bias. Therefore, present study was designed to assess the prevalence of TD in Indian subjects exposed to neuroleptics and to find out the role of various risk factors in their occurrence.

SUBJECTS AND METHODS

The sample population was chosen from patients attending Psychiatry OPD of GTB Hospital during two months of the study (October 2004 to November, 2004). Subjects were screened for exposure to neuroleptic drugs and those who have been using any of the antipsychotic drugs regularly for the past two years were included in this study after obtaining consent.

Information was gathered by history provided by the patient and a reliable informant along with physical

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examination of the patient and past medical records. Patients who were not having the drug prescriptions for last two years were excluded from the study so as the patients with spontaneous dyskinesias and withdrawal dyskinesias.

Final sample consisted of 62 patients and their age, sex, age of onset of illness, primary diagnosis, co-morbid psychiatric and medical illnesses, drug history with doses and family history of psychiatric disorders were noted.

To compare the effect of mean daily drug doses, mean doses of past two years were calculated by summing up each dose with the number of days of exposure for each drug and then dividing it by 730. e.g., if a patient has been exposed to risperidone 2 mg for 180 days, then to 1 mg for 180 days, then to 3 mg for past year, the mean dose was (2 X 180 + 1 X 180 + 3 X 365 / 730). Thus it provided the average daily dose of the drug taken be person. Two years period was taken because in the initiation and continuation phase of treatment drug doses were relatively higher than subsequent dosing. However, exposure to any drug for less than a month was ignored for the sake of statistical analysis. Presence of TD was diagnosed according to DSM-IV-TR criteria in all the subjects included in this study.

Statistical analysis:

For analysis subjects were divided into two groups- those having tardive dyskinesia and those without tardive dyskinesia. The age of onset of primary psychiatric illness, present age and differences in mean doses of drugs were compared by the independent t-test. Other categorical variables were assessed using Fisher's exact test . Finally, logistic regression was run taking tardive dyskinesia as dichotomous variable and co-morbidity, positive family history, exposure to risperidone, olanzapine, trihexyphenidyl and antidepressants as independent variables to predict the effect of these variables on occurrence of TD. SPSS version 13.0 for Windows was used to carry out analysis.

RESULTS

Prevalence of TD in our sample was 16.12%; they were more common in females *(P< 0.001)*; however there was no statistical significant difference *(P> 0.05)* between both the groups on the basis of age of onset of primary illness, age of onset of TD, primary diagnosis, co-morbid psychiatric or medical disorders and family history of psychiatric illness (Table 1).

Table 1
Distribution of Demographic and Illness Related Risk Factors

S.No.	Variable	Non TD (N=52)	TD (N=10)	
1.	Sex			
	Male	38 (73%)	1 (10%)	
	Female	14 (27%)	9 (90%)	P < .001
2.	Age	36.9 + 13.93	45 +10.68	p= 0.08*
3.	Age of onset of illness	29.6 + 13.7	33.8 + 9.89	p=0.36*
4.	Diagnosis			
	Schizophrenia	21 (41%)	2 (20%)	
	BPD	11 (21%)	3 (30%)	
	Depression with psy Feat	11 (21%)	2 (20%)	
	Other psychotic disorders	7 (13%)	2 (20%)	
	Somatoform & Anxiety disorder	2 (4%)	1 (10%)	*P* = 0.55
5.	Co-morbidity			
	HT	2 (4%)	0	
	DM	0	2 (20%)	
	Depression	7 (13%)	0	
	Substance Use	5 (10%)	0	
	Anxiety Disorders	3 (6%)	0	
	Epilepsy	1 (2%)	0	*P*= 0.01
6.	Family History			
	Depression	4 (8%)	1 (10%)	
	MDP	3 (6%)	1 (10%)	
	Schizophrenia	2 (4%)	1 (10%)	
	Epilepsy	1 (2%)	0	*P*= 1.00

* Independent sample t test, Rests are Fisher's Exact test

Table 2
Average Daily Doses of antipsychotics and antiparkinson drugs in both groups

S. No.	Drug	Non TD (N=52)	TD (N=10)	p*
1.	Risperidone	3.3 + 2.2 (44%)	3.5 +2.0 (60%)	0.8
2.	Olanzepine	6.7 + 5.3 (35%)	7.5 + 3.5 (20%)	0.8
3.	THP	4.0 +1.6 (29%)	3.8 + 1.3 (60%)	0.8

* Independent sample t test; Figures aside indicate number of people exposed to respective drugs

Table 3
Odds Ratio Values of Risk Factors on Occurrence of TD

S. No.	Variable	Significance	Odds Ratio	95% CI	
				Lower	Upper
1.	Co-morbidity	0.714	0.70	0.10	4.71
2.	Family History	0.206	1.66	0.75	3.63
3.	Risperidone	0.216	3.15	0.51	19.41
4.	Olanzapine	0.118	2.28	0.81	6.42
5.	Trihexyphenidyl	0.102	3.74	0.76	18.22
6.	Antidepressant	0.583	0.59	0.09	3.77

We did not find any patient using conventional neuroleptics because we stressed on the medical records of past two years. However, most of the patient had long term illness (average approximately 10 years), exposure to conventional neuroleptics could not be ruled out and result must be interpreted with caution. We also analyzed whether different daily doses of Risperidone, Olanzapine, and Trihexyphenidyl affect the development of TD, but did not find any significant difference *(P> 0.05)* between groups (Table 2). Other drugs used by samples were as follows- Aripiprazole to 14% and 20%, clozapine to 2% and 0; Valproate to 27% and 2%; Lihium to 8% and 30%, Fluoxetine to 20% and 10%; Escitalopram to 15% and 20%; and other antidepressants to 15% and 0 subjects in Non-TD and TD group respectively.

Classification of the study group was 87.1% during the logistic regression. Risk of development of tardive dyskinesia was negatively associated with co-morbidity and exposure to antidepressant while positively associated with family history of psychiatric disorders, and exposure to risperidone, olanzapine and trihexyphenidtl (Table 3). However, none of these variables reached statistical significance.

DISCUSSION

Previous studies on Indian population have reported a prevalence of 10%[3] and 29%[4] for drug induced tardive dyskinesia. Prevalence found in present study is lower than described by Bhatia et al[4], probably because they have included schizophrenic patients which usually require higher doses and are often exposed to conventional antispyhotics. In this study, exposure to neuroleptic was the only criteria for inclusion without being affected by diagnosis and duration of treatment. Therefore average doses of antipsychotics were relatively lower and all the subjects were on atypical drugs for at least past two years thus contributing to lower incidence[5,6] . Moreover, our findings go along with the previous reports of ethnic variation[7] where lower rates of TD have been described in Asian subjects[1]. However at this point, we are unable to comment which of these factors played major role for such low incidence, and it requires further study.

Female subjects in this study suffered higher rates of dyskinesias. It has been described as an important risk factor in literature but few studies did not find any evidence in its favor[8,9] and one even reported higher incidence in males[4]. In a review article, Sachdev[1] suggests that it is not only the gender but 'age- gender interaction' that works behind increased prevalence of TD in females. Post-hoc analysis of our data found that females were older (44.13+ 14.69) than males (34.15 + 11.97) *(P=0.008)*. Thus we also opine that age-gender interaction may be more important for development of TD, rather than any of the factors alone.

Age has been described as the most important risk factors across studies[1,9-12]. Higher prevalence with increasing age can be attributed to age related brain degeneration[13], neurological pathologies[14], co-morbid medical disorders[14], longer years of treatment[8,12] and thus higher cumulative neuroleptic doses[1] and spontaneous dyskinesias[14]. However, we did not find any effect of age on the prevalence of dyskinesia in the whole sample. Similar results were reported in other studies[4,8]. It is possible that there is a cut-off point of age beyond which the

risk of TD increases as described by Woerner et al[2] who demonstrated that risk of TD increases after 50 years even on the lower doses of antipsychotics and despite the facts that younger subjects had longer exposure to neuroleptics. The mean age of subjects in our sample was lower than this cut off point. Secondly, as we have mentioned, according to us, age and gender interaction is the root cause for development of TD, rather than any of the factors alone.

Illness related factors that increase the risk of TD are early age of onset of primary illness[15], presence of mood disorders in the patient[1,4,11], history of substance use[12] and family history of mood disorders[1]. However, we could not confirm any of the findings (in-fact co-morbidity and exposure to antidepressants were negatively associated with risk of TD) except for the family history of psychiatric illness which enhanced the risk (but statistically insignificant). Similar results have been found in other studies which could not correlate it with primary diagnosis[8-10], and age of first exposure to antipsychotic[10].

Not only the psychiatric disorder but presence of medical disorder- particularly diabetes mellitus may be associated with increased risk[16]. However, our findings do not support it and confirm findings of Miller et al[12].

Lastly, drug related factors e.g., exposure to conventional neuroleptics[8], higher cumulative doses or longer duration of treatment[8,10,12] and use of antiparkinsons drug[15] have been reported to increase the risk of TD. In this study we found that the doses of antipsychotics and trihexyphenidyl did not affect TD, Though those with TD had more chances to be exposed to trihexyphenidyl and atypical neuroleptics (but statistically insignificant). However, due to past history of exposure to conventional antipsychotic for pretty long period, validity of this finding can be challenged.

This study had few methodological limitations- exclusion criteria cut down the sample to small size in present study. Though in this sample we did not have any subject with the history of conventional drug use in past two years, such possibility can not be ruled out before that. Moreover, the mean daily doses of drugs were also low due to sample with mixed diagnosis. Our results have probably been affected by the lower mean doses of the drugs, use of atypical antipsychotics in past two years that are known to reverse TD[5-6] and use of concomitant trihexyphenidyl that can have a protective effect. As hypothesized at inception, we did not find any evidence that antidepressants increase rate of TD and go along with previous finding[10].

In conclusion, this study confirmed that female gender with advancing age is the only risk factors for TD and it is unaffected by presence of other disorders, doses of atypical neuroleptics and exposure to other psychotropic drugs. Due to small size of sample, results must be generalized with caution and further research is required with methodological improvements.

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STATEMENT OF INTEREST

There are no conflicting interests to declare as study was not funded by any agency.

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