Original Article

A Survey of the Tardive Dyskinesia Induced by Antipsychotic Drugs in Patients with Schizophrenia

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Objective: Tardive Dyskinesia (TD), is one of the important problems of the patients with schizophrenia. The emergence of these side effects depends on so many factors such as the patients' age and the duration of antipsychotic treatment. By discovering new drugs (Atypical), there has been an outstanding decrease in the emergence of these side effects. The present study investigates the symptoms of TD in the Patients with schizophrenia who were under treatments for more than 6 months.
Method: The sample of this study was 200 Patients with schizophrenia of four wards in Razi hospital (two acute and two chronic wards) who were hospitalized in the winter of 2006 and were qualified for this study. The subjects were 101 males and 99 females who were younger than 60 and had received antipsychotic drugs for at least 6 months. After psychiatric interview and filling the demographic questionnaire by the patients, the required information about the drugs and the intensity of the symptoms was acquired. Then clinical and physical examinations of tardive dyskinesia were done. Next, the tardive dyskinesia disorders' check list (AIMS) was used. Findings of this cross-sectional, descriptive study were analyzed by SPSS.
Results: There was a high ratio of 95% between TD and the age factor (P=0.05). There was no relationship between symptoms frequency and duration of treatment (P=0.68). Facial muscles and oral zones were mostly involved in T.D disorder (72%).
Conclusion: No significant difference was observed between nine fold symptoms of T.D in patients who were using traditional drugs and those who were using the new ones (typical and atypical). Findings showed that in the intensity of the symptoms, gender does not play a major role.

Key Words: *Drug-induced dyskinesia, Anti-psychotics agents, Schizophrenia,*

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With the emergence of antipsychotic drugs and a considerable improvement in Patients with schizophrenia, new horizons were opened in the psychiatric science (1). Despite their effectiveness, these drugs have various side effects particularly Tardive Dyskinesia disorder which is associated with certain difficulties (2). TD induced by antipsychotic drugs is a disorder which appears late (at least three months after consuming them) as involuntary movements and is in the form of choreoathetoid and remains at least for 4 weeks. The most prevailing of these movements are at the areas of mouth and face though the other muscles may also be involved (3-5).
At least 20-30% of patients who use antipsychotic drugs show TD symptoms .The patients suffer from these movements (6). They also create a psychological fatigue in those who take care of these patients .Depending on the affected area, it creates certain inabilities (7).While the muscles of the mouth and the face are involved, the patients have difficulty in speaking and swallowing .In developed and critical cases, it entangles the respiratory organs and endangers life (8). Therefore, an on-time diagnosis and treatment of the disease is important in the increase of receiving the treatment and reduction of patients' sufferings and anxieties (9). In a 32-month follow up of 101 Patients with schizophrenia, the individuals with TD showed a higher rate of respiratory infections and cardiac or blood vessels diseases(10) and Type 2 of Dopamine receptors is mentioned as a creating factor of the disorder .Therefore, the new medicines with less control on these receptors are more suitable to reduce the movement disorders (11) .However, there have

been many reports indicating the TD while using the new. (Atypical) medicines (12). Some of the risk factors of TD disorders are:
1) Long treatment with antipsychotic drugs
Aging
2) Gender and type of antipsychotic drugs (13)
3) In order to make the diagnosis and appropriate assessment and on time interference, the Abnormal Involuntary Movement Scale (AIMS) is used which makes a general assessment of the patients who consume antipsychotics in 3 to 6 months intervals to diagnose the movement disorders (14, 15). There are also other studies which indicate that all TD cases should not be attributed to antipsychotic medicines (16) and that other factors such as basal brain and endocrine system disorders should also be considered (17). In recent decade, many studies have been conducted on the emergence, risk factors, and intensity of symptoms of these disorders (18, 19) .No matter what causes TD, it needs specific treatment (20).
Considering the new antipsychotic drugs and the ongoing development in this field and due to the fact that by using them we can reduce the TD, we decided to not only investigate the frequency and distribution of the intensity of symptoms and signs of TD in acute and chronic patients with schizophrenia, but also compare the traditional drugs with the new ones that are made in Iran for the patients with schizophrenia for the Iranian community.
Upon the previous studies, the present study investigates the symptoms of TD disorders by using AIMS and emphasizes the necessity of using it for the patients with schizophrenia who undergo antipsychotic treatments for more than 6 months.

Materials and Method

This study was conducted on those (male and female) who have consulted with the staff of Razi Psychiatric Hospital and been diagnosed as having Schizophrenia according to the psychiatric interview and DSM-IV-TR standards. The patients were admitted in the wards of Qanoon (Acute Unit for female), Sina (Acute Unit for male), Farabi (Male Unit) and Aboureihan (Female Unit). The inclusion criteria in research were as follows :
1) Patients should have been under the treatment by neuroleptic medicine for at least six months. The dose and type of the drugs should be determined.
2) Their age should be less than 60.
3) The Schizophrenia diagnosis should be based on DSM-IV-TR standards and to be confirmed by two psychiatrists .
4) The patients are to be admitted in hospital for at least 6 months and have gone under treatment and investigation to find out the side effects of the so-called drugs .
The exclusion criteria of the research were as follows :
1) If any TD symptoms were observed before the drug prescriptions.
2) Patients with Mental retardation
3) Patients with Thyroid disorders
4) Patients with TD induced by basal ganglia such as Huntington-Wilson and Sydenham Chorea
5) The patients who were admitted to hospital for at least 3 months and have gone under treatment and investigation to find out the side effects of the so-called drugs .
The researchers considered last years antipsychotic drugs used by the patients admitted in the acute ward and included them along with the other drugs used in this 6 -month period of the study but for the patients of the chronic ward, they considered both last years drugs and the drugs used in the last 6 months before the study began, and included all of them during the present study. It is worth mentioning that in spite of introducing new atypical antipsychotic drugs in recent years, most of the patients still tended to use traditional drugs.
All the existing drugs in the Iranian pharmaceutical system are called traditional antipsychotic drugs.
Traditional antipsychotic drug's dose is equal to 10-15Mg Haloperidol , and the new antipsychotic drug's dose is equal to 4-6Mg Risperidone and 10-15Mg Olanzapine.
At the first stage, 250 patients were selected but 50 patients were dropped according to the standards of inclusion and exclusion, and 200 patients (99 female and 101 male) were remained. In order to collect the data, the following instruments were used :
Demographical questionnaire: The questionnaire contains data such as age, gender, type of the medicine, duration of medicine consumption, duration of admission, education, etc . Clinical examination was made based on DSM-IV-TR standard to diagnose TD .
Ranking checklist for AIMS (21): The intensity of TD is specified in 9 sub-groups. (Ranging from S1 to S9). Each sub-group has scores from 0-4. They have been defined as follows : Zero (without any symptom); one (minimum symptoms) ; two (slight symptoms); three (average); and four (intensive symptoms).
The range of scores is 0-36 and the patient should not have anything in his/her mouth such as chewing gum or chocolate .
After examining the patients and a psychiatric interview and confirmation of Schizophrenia, demographical questionnaire was also completed by the reasearches.Then; clinical examination based on DSM-IV-IR standards was made to find out TD. In the next stage, those groups of the patients with TD were evaluated using the ranking checklist of AIMS .
In order to analyze the data to achieve the objectives of the research, the correlation coefficient of Pierson, and independent T-test were used and the results were analyzed using SPSS software .

Ethical consideration

In addition to obtaining satisfaction of the patients' families and the patients themselves, they were assured that the data would be kept confidential.

Table 1: Frequency Distribution of Tardive Dyskinesia in patients with Schizophrenia

State	Frequency	Percent
TD (+)	78	39
TD (-)	122	61

Table 2 -The 9 Fold Symptoms of Tardive for Antipsychotic Medicines

symptoms	Position	Frequency	Percent
S1	+	9	4.5
	-	191	95.5
S2	+	30	15
	-	170	85
S3	+	56	28
	-	144	72
S4	+	37	18.5
	-	163	81.8
S5	+	23	11.5
	-	177	88.5
S6	+	39	19.5
	-	161	80.5
S7	+	27	13.5
	-	173	86.5
S8	+	28	14
	-	172	86
S9	+	23	11.5
	-	177	88.5

S3 with 28 %is the highest and S1 with 4.5 %is the lowest.
S1<S5=S9<S8<S2<S4<S5<S3

Results

At the beginning, the descriptive findings of the sample under investigation are discussed. Men and Women under investigation did not have meaningful statistical differences (49.5 %for women and 50.5 %for men .)The results showed that the youngest and the oldest were 19 and 60 respectively .Using the average, mean and standard deviation, age of the half of the sample group was 44 or less.

Concerning the beginning of the disease and receiving medical treatment, the average of 12.89 years passes from the beginning of the diagnosis and start of taking medication .

With regard to the frequency distribution and consumption of antipsychotic medicines that was discussed before, consumption of medicine was started at the period of study or at least 6 months before that . Atypical medicines are medicines which had existed in Pharmacopoeia of Iran in 2005.

Most of the patients use the traditional or typical antipsychotic medicines .In the study of the frequency, by doing individual clinical examinations (presented in Table 1), TD symptoms are considerable.

In Table 2, it has been specified that between the frequencies of the two tested groups who use typical/atypical medications, no significant statistical differences were found in the 9 fold symptoms of Tardive at the significance level of 95 %.

The contemplating point is that in the sample under investigation, no difference was observed between the intensity of Tardive Dyskinesia (TD) symptoms and

Table 3: The Intensity of TD in Schizophrenic Women and Men

Sign		Drug type		Indepe t t-test	Significance level
		Atypical	Typical		
S1	Female	0.16	0.79	-0.15	0.88
	Male	0.18	0.79		
S2	Female	0.67	1.48	1.49	0.14
	Male	0.40	1.1		
S3	Female	1.18	1.81	1.13	0.26
	Male	0.92	1.59		
S4	Female	0.58	1.39	-0.61	0.545
	Male	0.69	1.35		
S5	Female	0.29	1.01	-1.38	0.17
	Male	0.51	1.25		
S6	Female	0.85	1.61	1.32	0.19
	Male	0.57	1.31		
S7	Female	0.57	1.36	0.77	0.44
	Male	0.43	1.20		
S8	Female	0.66	1.46	1.31	0.193
	Male	0.41	1.20		
S9	Female	0.40	1.21	-0.41	0.68
	Male	0.48	1.26		
Total	Female	5.35	8.82	0.81	0.42
	Male	4.43	7.21		

AIMS scores in schizophrenic men and women .In Table 3, this point is presented in details .

Lastly, in Table 4, it is observed that between the age of patients and duration of consumption of antipsychotic medicines with frequency of TD symptoms, there is a meaningful relation at the level of 95,% while there is not such a relation between the frequency of TD and duration of medicine consumption..

Discussion

Introducing antipsychotic medicines opened a new horizon to treat patients with schizophrenia (20). The antipsychotic medicines have some side effects such as TD disorders which appear later than others (3). Before 1950s, when antipsychotic medicines had not been discovered, movement disorders were also reported in chronic patients with schizophrenia (14). Therefore, antipsychotic medicines are not the only risk factors.

Before examining the TD disorders, we should consider their existence while diagnosing the disease and consider their appearance along with some other diseases in patients with schizophrenia (15). In a study that was conducted on 88 patients with schizophrenia in Estonian hospital, it was shown that the spread of TD disorder resulting from antipsychotic drugs was 32.3% and that 38.4 %of the movement disorders were not resulting from the medicines (21). In the present study, the frequency of TD resulting from antipsychotic medicine was 39 % which is not considered a significant difference .Depending on the entanglement of the muscles of different areas, different side effects are observed (4).

Involvement of the muscles of mouth and face which is the prevailing area of infection makes a disruption in speaking and swallowing (19). In a research conducted in 1992, 30 patients out of 919 of TD patients had involvement of muscles of mouth and face (6). In the

present study, the sub-group of S3, which has the highest involvement of the facial and mouth muscles, has the highest frequency of 28%.

In the previous studies, emphasize was on involvement of muscles of the body organs and then respiratory muscles (5, 18).In the present study, the muscles of body with 19.5 % have the highest prevalence frequency in the second rank. The previous studies showed that TD disorders among women are more than men but in this study there was no significant difference between TD disorder's symptoms in male and female patients with schizophrenia. Holi et al. (2004) showed that the TD symptoms are created just in 10% of those who use Clozapine (22). Nearly two-thirds of the patients suffer from a neuroleptic-induced movement disorder despite the relatively low antipsychotic doses and the use of anticholinergics (23, 24). This study shows that there is no significant difference in a comparison between typical and atypical medicines and the nine-fold detachment. Although significant difference exists among the age of the patients, the duration of drug consumption, and the frequency of TD symptoms at the level of 95%, there is no such a relation between TD symptoms and dose of the drug.

The main limitations of this study are connected to the lack of precise information on the dose of drugs used by the schizophrenic patients within the last year. Considering that anti-parkinson drugs can also create these symptoms, all the patients with schizophrenia used antipsychotic drugs along with anti-extra pyramidal drugs that intensify the symptoms.

Considering that on-time diagnosis results in appropriate treatment of TD (5-40%), periodical examination of patients with schizophrenia who consume antipsychotic drugs for more than 6 months is suggested.

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