

Cognitive Dysfunction in Tardive Dyskinesia

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Tardive Dyskinesia is a serious, long term side effect of chronic neuroleptic treatment. The magnitude of this iatrogenic health problem has been compounded by the inadequate treatment currently available. All schizophrenic patients residing in the three main hospitals in Alexandria with Psychiatric inpatient units were studied during May and June 1988. The aim of this work was to detect Tardive Dyskinesia (TD) among schizophrenic inpatients and to study the relationship between TD and cognitive impairment. Only cases fitting the DSM III diagnostic criteria for schizophrenia and who were under neuroleptic treatment for more than one year were included in this study (280 patients, 161 males and 119 females). The study showed that TD prevalence rate among the schizophrenic population was 4.2% (lips and perioral movements in 58.3% and tongue movements in 41.6%). Patients with TD performed significantly lower than patients without TD on the comprehension, digit span and similarities subscales of Wechsler Adult Intelligence Scale ($t = -3.51$, -6.022 and -3.26 respectively).

All the correlations between scores on comprehension and digit span subscales and lip movements were statistically significant ($r = 0.467$ and 0.622).

(Egypt. J. Psychiat., 1993, 16:113-120).

Introduction

The introduction of effective antipsychotic drugs in the early 1950s has led to rapid control of psychotic symptoms and behaviors in a wide variety of psychotic illness. Virtually all the antipsychotic agents exert undesirable neurological effects. Hence the name of "neuroleptic" is applied to this group of drugs. (Baldessarini et al, 1980).

Tardive Dyskinesia (TD) is the most feared complication of antipsychotic medications because the symptoms are frequently persistent and often permanent. (Fann, 1984)

TD by definition is an iatrogenic disease due to long term administration of

neuroleptic agents. (Klawans, et al 1980). The classic signs of TD is a triad of cheek- face- tongue movements, often called the bucco-lingual masticatory syndrome. (Fann, 1984). In addition TD can display choreiform movements of the hands and feet, athetoid movements of the extremities, and dystonic posturing of the neck and trunk (Casey, 1987)

The observation that TD is frequently permanent even after discontinuation of antipsychotic drugs has led investigators to search for structural alterations in the brains of patients with TD (Gelenberg, 1976). Christensen and associates (1970) have reported the presence of neuronal degeneration and gliosis of the substantia nigra in 27 out of 28 brains of TD patients. 21 cases of them, were attributed to antipsychotic drugs. (Christensen, et al., 1970). There is substantial evidence

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that the pathogenesis of TD relates to chronic dopamine receptor site blockade, the pathophysiology of the disorder relates to the resultant receptor site supersensitivity. (smith et al, 1977; Granacher et al.,1981)

The aim of this work is to detect TD among schizophrenic inpatients in Alexandria Hospitals. Also to find the relationship between TD and cognitive dysfunctions in the collected TD schizophrenic patients.

Subjects and Method

All schizophrenic patients residing at El-Mamoura Mental Hospital, the Psychiatric Unit of Alexandria University Hospital and the Health Insurance Hospital "Gamal Abdel - Nasser" during May and June 1988 were examined. All patients were verifying the DSM III diagnostic criteria for schizophrenia (APA,1980). They were under neuroleptic treatment for more than one year.

The total number of patients examined were 280 (161 males and 119 females). Their distribution among the hospitals were as follow: 251 at El-Mamoura Mental Hospital. 15 patients at Alexandria University Hospital and 14 patients at Health Insurance Hospital.

The whole schizophrenic population was scrutinized to detect cases with Tardive Dyskinesia (TD). A clinical judgement ran hand in hand with the application of Abnormal Involuntary Movement Scale ,AIMS, (ADAMHA,1974). The diagnosis of positive cases of TD was based on TD research criteria proposed by Schooler and Kane. (Schooler et al., 1982).

Patients group:

Twelve subjects suffering from TD were identified. 7 males and 5 females.

Control group:

A control group of 12 schizophrenic

patients who were residing in the same hospitals, had no TD and were under medication for more than one year (7 males & 5 females).

The patients and control group were subjected to the following:

I. Clinical Examination

A. Demographic data.

B. Psychiatric interview.

C. Drug history.

D. Neurological examination.

II. Psychometric Examination:

A. Wechsler Adult Intelligence Sub-scales which includes:

1. Comprehension, 2. Digit span

3. Similarities.

B. Scale for the assessment of thought, language and communication (TLC). (Andreason, 1979).

III. Statistical Analysis:

The tests used for analysis and correlation of data were mean (x), standard deviation (SD), t-test, z-test and correlation / regression analysis "n".

Results

Tardive Dyskinesia (TD) prevalence rate among the schizophrenic population was 4.2%. Lips and perioral area movements occurred in 7 patients (58.33%), tongue movements in 5 (41.62%), Jaw movements in 3 (25%), choreoathetoid movements of the upper extremities were present in 2 patients (16.67%), while movements of the lower extremities (Piano-Player movements) were present in 3 patients (25%). No abnormal involuntary movements were detected in muscles of facial expression or those of the trunk.

The mean age of TD patients was 42.58 ± 11.07 , while the mean age of non TD patients was 38.08 ± 9.95 ($t = 1.0473$, insignificant).

The mean duration of illness of TD patients was 16.83 ± 10.23 years, while

the mean duration of illness of non TD patients was 10.92 ± 7.6 years ($t = 1.606$ insignificant). The mean duration of neuroleptic treatment in TD group was 16.17 ± 9.91 years while the mean duration of neuroleptic treatment in non TD group was 10.83 ± 6.79 years ($t = 1.54$, insignificant).

The mean value of current daily dose of neuroleptic treatment in chlorpromazine equivalent doses of neuroleptic treatment of TD patients was 387.08 ± 229.45 mg, while that dose of non TD patients was 339.17 ± 251.19 ($t = 0.487$, insignificant).

Eight patients with TD were currently receiving antiparkinsonian drugs, while 9 patient without TD were receiving such treatment ($z = 0.449$, insignificant).

Abnormal "hard" neurological signs were detected in 5 patients with TD (41.67%) and only in 2 patients without TD (16.67%) ($z = 1.347$, insignificant).

Patients with TD performed significantly lower than patients without TD on the comprehension, digit span, and similarities subscales of Wechsler Adult Intelligence Test ($t = 3.51$, -6.022 and -3.257 respectively).

Only "self reference" as a formal thought disorder was significantly more frequently encountered among TD group than the non TD group ($z = 2.108$).

Flat affect was positively correlated with tongue movements ($r = 0.447$) and the duration of neuroleptic treatment correlated positively with tongue movements ($r = 0.419$).

The correlation between the scores on comprehension and digit span subscales and lip movements were statistically significant ($r = 0.467$ and 0.622).

Positive correlation between destruct-

ible speech and lip movements and loss of goal and tongue movement were found ($r = 0.470$ and 0.655). A distinctive negative correlation between perseveration and lower limb movements was found ($r = 0.507$).

Discussion

The present study showed the prevalence rate of TD to be 4.2%. Kane and Smith (1982) reviewed 56 prevalence surveys of TD in neuroleptic treated inpatients and found vastly different prevalence rates with a mean of 20%.

Okasha et al (1986) found a prevalence of 1.7 % in neuroleptic treated Egyptian patients. The low prevalence rate in Egyptian studies may be due to the irregular intake of neuroleptics.

There is wide controversy as regards the relation between Tardive Dyskinesia and anti-parkinsonian treatment. Several studies did not find a relation between TD and anti - parkinsonian treatment (Mukherjee et al, 1982, Mallya et al, 1979). Other studies have implicated antiparkinsonian medication in increasing the risk of TD. (Chouinard, et al., 1979; a&b). The present study showed that there is no significant difference between the TD group and the non TD group as regards the intake of antiparkinsonian treatment.

In agreement with other studies done by Josec et al (1979) and Mukherjee et al (1982) the present study showed a positive relation between older age and increased risk of TD "mean age of TD was 42.58 ± 11.07 years".

The duration of neuroleptic treatment of TD group was higher in the present study than that of the non TD group ($t = 1.54$). One study demonstrated a significant association between TD and the duration of neuroleptic treatment Gardos

Table 1
Antiparkinsonian Treatment, Negative Symptoms, Neurological Signs, Drug History and Result of WAIS among Schizophrenic Patients With and Without TD

	TD group		Non TD group		Z - test
	No	%	No	%	
With antiparkinsonian	8	66.67	9	75	- 0.449
Without antiparkinsonian	4	33.33	3	25	0.449
Negative symptoms					
Flat affect	11	91.67	4	33.33	2.95*
- Lack of initiation	7	58.33	6	50	0.409
- Poor self care	4	33.33	3	25	0.449
- Poor non verbal communication	4	33.33	1	8.33	1.508
Neurological signs:					
+ ve neurological signs	5	41.67	2	16.67	1.347
- ve neurological signs	7	58.33	10	83.33	-1.347
Drug history:	Mean	SD	Mean	SD	
- Duration of intake/year	16.17	9.91	10.83	6.79	1.54
- Current daily dose in CPZ/Equ	387.08	229.45	338.17	251.19	0.487
WAIS results:					
- Comprehension	3.42	1.62	7.33	3.5	-3.51*
- Digit span	5.17	1.64	9.83	2.12	-6.022*
- Similarities	7.08	2.64	10.33	1.97	-3.257*

WAIS: Wechsler Adult Intelligence Subscales.

CPZ Equ: Chlorpromazine Equivalent dose.

Table 2
Pearson Correlation Relationship Between The Distribution of Involuntary Movement and Drug History
Antiparkinsonian Treatment, Negative Symptoms In WAIS Subs

	Lips	Tongue	Jaw	ULS	LLS	AI
Duration of neuroleptic treatment	0.177	0.169	0.419*	0.018	0.287	0.311
Daily dose of neuroleptic treatment	0.181	-0.093	-0.054	0.042	0.213	0.103
Antiparkinsonian treatment	0.193	-0.265	-0.035	0.138	0.243	-0.092
Neurological examination	0.395	0.053	0.312	-0.193	0.053	0.275
Flat affect	0.308	0.447*	0.293	0.234	0.033	0.602*
Poor non-verbal communication	0.348	0.178	-0.194	-0.1155	0.427	0.308
Lack of Initiation	0.038	-0.048	-0.158	-0.025	-0.158	0.084
Poor Self care	0.193	0.053	0.035	-0.193	0.035	0.092
Comprehension	-0.467*	-0.273	-0.121	-0.081	-0.314	-0.600*
Digit span	-0.622**	-0.283	-0.209	-0.243	-0.209	-0.743*
Similarities	-0.127	-0.177	-0.099	-0.339	-0.403	0.570*

et al., (1980). Several other studies did not find any evidence that patients with involuntary movements have received longer treatment with neuroleptics (Waddington et al., 1987; Thomas and McGuire, 1986).

Positive "hard" neurological signs were more present in our TD group than in non TD group ($z = 1.347$). Earlier studies in 1970 found an increase in hard (i.e. localizing) as well as soft "non localizing" signs of neuroleptic abnormalities in schizophrenia. (Gaultier et al., 1984). It has been suggested that "soft" signs are not only non specific but possibly medication induced. (Woods et al., 1986). Nevertheless Kolakowska et al (1985) found that "soft" signs were no more frequent among schizophrenic patients with TD as compared to those without TD.

In the present study flat affect as a negative schizophrenic symptom was significantly higher among the TD group than the non TD group ($z = 2.95$). This finding was in accord with other studies who have found TD to be commoner in patients with negative symptoms. (Waddington et al., 1986; 1987)

The present study showed that TD group got significantly lower scores than non TD group on Wechsler comprehension subscale ($t = 3.51$). Comprehension is a test of common sense judgement and practical reasoning (Lezak, 1983). This demonstrates that cognitive deterioration is associated with TD.

The score of TD patients was significantly lower than those of non TD patients on the digit span subscale ($t = 6.022$). Digit span is a test for recent memory and attention. Thomas and McGuire (1986) reported that their TD

patients performed poorly on tests of delayed recall and concluded that TD may be associated with poor short term memory. The performance of TD group on Wechsler's similarities (test of verbal concept formation and general intellectual ability) subscale was significantly lower than non TD group ($t = 3.257$).

We may conclude from this that the TD group who performed poorly on the 3 WAIS subscales positively have an organic brain lesion. Donnely et al (1980) found that schizophrenic patients with abnormal brain CT "computerized tomography" performed significantly worse than the remaining schizophrenic patients in Halstead-Reitan and Wechsler Adult Scale. Also on CT brain studies. Bartels and Themelis (1983) demonstrated structural abnormalities in the basal ganglia of patients with Tardive Dyskinesia.

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Les Disfonctionnements Cognitifs dans La Dyskinésie Tardive.

La dyskinésie tardive est un sérieux effet secondaire à long - terme du traitement chronique avec les neuroléptiques.

La magnitude de ce problème iatrogénique a été aggravé par l'insuffisant traitement actuellement disponible.

Tous les malades schizophrènes habitent dans les trois principaux hopitaux qui contiennent des unités pour les malades psychiatriques hospitalisés. Ils ont été étudiés pendant les mois de Mai et de Juin, 1988.

Le but de ce travail est de détecter la dyskinésie tardive (DT) entre les malades hospitalisés schizophrènes et d'étudier la relation schizophrènes d'étudier la relation entre DT et la dysfonctionnement cognitive.

Les cas convenant les critères diagnostiques du DSMIII pour la schizophrénie et qui étaient sous le traitement avec les neuroleptiques pour plus d'un an ont participé dans cette étude (280 malades, 161 mâles et 199 femelles)

Cette étude a montré que le pourcentage de prévalence de la DT parmi la population de schizophrènes a été 4,2% (mouvements périoral et mouvements de lèvres chez 58,3% et mouvements de langue 46%)

Les malades avec la DT ont de significatifs résultats plus bas que les malades sans DT. Ceci concerne les sous-série de la compréhension, les chiffres étendus et les similaires de la série de l'intelligence des adultes de wechsler.

($t = 3.51, 6.022$ et 3.26 respectivement) Tous les corrélations entre les résultats des sous - séries de la compréhension, des chiffres étendus et des mouvements de lèvres sont statistiquement significatifs ($r = 0.467$ et 0.622).

الاختلال المعرفى فى الاضطراب الحركى اللا إرادى المتأخر

تم تقييم كل المرضى الفصامين الموجودين فى ثلاثة مستشفيات نفسية فى مدينة الاسكندرية خلال مايو ويونيه ١٩٨٨، وكان الفرض من هذا التقييم تحرى وجود اضطراب الحركة الإرادى المتأخر الظهور المصاحب لتناول عقاقير المهدئات العظمى لفترات طويلة وكذلك دراسة العلاقة بين وجود هذه الحركات وبين اضطراب القدرات المعرفية، وقد تم تشخيص هؤلاء المرض طبقاً لدليل التشخيص الأمريكى الثالث المراجع.

وقد أظهرت النتائج أن معدل إنتشار هذه الحركات فى المرضى الفصامين حوالى ٤.٢٪ كما أشارت النتائج أن المرضى الذين أظهروا هذه الحركات اللا إرادية قد كان أدائهم أقل بدالة إحصائية ملحوظة على الاختبارات الفرعية لقياس وكسلر لكاء الراشدين والبالغين وهى الفهم - الأرقام و المتشابهات، كما ناقشت الدراسة أهمية هذه النتائج من النواحي الإكلينيكية والبحثية.