Dusunen Adam The Journal of Psychiatry and Neurological Sciences 2016;29:60-66
DOI: 10.5350/DAJPN2016290106

Brief Report / Kısa Araştırma

Tardive Dyskinesia in Mentally Retarded Patients under Long-Term Antipsychotic Treatment

Aylin Can[1], Ahmet Nalbant[1], Huseyin Sehit Burhan[1], Alparslan Cansiz[1], Kaasim Fatih Yavuz[1], Mehtap Arslan Delice[1], Erhan Kurt[1]

[1]*Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Istanbul - Turkey*

ABSTRACT

Tardive dyskinesia in mentally retarded patients under long-term antipsychotic treatment

Objective: Tardive dyskinesia (TD) is an iatrogenic movement disorder, developing due to prolonged use of dopamine receptor blocking agents, that may affect various parts of the body. In a number of studies, prevalence rates between 5 and 30% have been reported. This study aims to research TD in patients with mental retardation who have been hospitalized for a long time and medicated regularly.

Method: Included in this study were 40 patients with a diagnosis of mental retardation comorbid with schzophrenia or other psychotic disorders according to DSM-IV TR that had been hospitalized in the chronic patients' ward of Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery for a long period. Duration and type of antipsychotics both at the time of interview and over the preceding years were recorded. Dyskinesia was assessed using the Abnormal Involuntary Movements Scale (AIMS). We also used the Simpson–Angus Rating Scale (SAS) for Parkinsonism. Akathisia was measured using the Barnes Akathisia Rating Scale (BARS).

Results: According to AIMS scores, 9 participants (22.5%) received a diagnosis of TD. There was no significant correlation between the type and duration of ongoing or the longest used treatment and the prevalence of TD. There was a statistically significant correlation between the participants' age and TD (p=0.009). There were no gender differences for TD

Conclusion: We found that long-term use of antipsychotics is unrelated with TD, while age is an important risk factor for TD. It can be said that switching from first generation to second generation antipsychotics does not reduce the prevalence of TD.

Keywords: Antipsychotics, mental retardation, tardive dyskinesia

ÖZET

Uzun süre antipsikotik tedavisi alan mental retardasyonlu hastalarda tardif diskinezi

Amaç: Tardif diskinezi (TD) uzun süreli dopamin reseptör blokajı oluşturan ilaçlara bağlı olarak gelişen, vücudun çeşitli bölgelerini tutabilen iatrojenik bir hareket bozukluğudur. Yapılan çalışmalarda prevalansının %5 ila %30 aralığında değiştiği görülmektedir. Bu araştırma, ruh sağlığı hastanesinde uzun süredir yatan ve düzenli olarak ilaç almakta olan mental retardasyonlu hastalarda tardiv diskineziyi araştırmayı amaçlamaktadır.

Yöntem: Bu çalışmaya Bakırköy Ruh ve Sinir Hastalıkları Hastanesi kronik servislerinde uzun süredir yatmakta olan ve DSM-IV TR'ye göre mental retardasyon ve eşlik eden şizofreni veya diğer psikotik bozukluk tanısı alan 40 hasta dâhil edildi. Hastaların halen kullandıkları antipsikotik türü (birinci kuşak ve ikinci kuşak) ve süresi ile geçmişte en uzun süre kullandıkları antipsikotik türü ve süresi incelenmiştir. Tardiv diskineziyi saptamak amacıyla Anormal İstemsiz Hareketler Ölçeği (AİHÖ) kullanılmıştır. Ek olarak Barnes Akatizi Ölçeği (BADÖ) ve Simpson-Angus Nöroleptiklere Bağlı İstemsiz Hareket Bozukluklarını Değerlendirme Ölçeği ile akatizi ve parkinsonizm varlığına bakılmıştır.

Bulgular: AİHÖ puanlarına göre değerlendirildiğinde katılımcıların 9'una (%22.5) TD tanısı kondu. TD tanısı konanlarda geçmişte ya da halen kullanılan antipsikotik türü ve süresi ile TD arasında bir ilişki saptanmadı. Katılımcıların yaşlarıyla TD arasında istatistiksel olarak anlamlı ilişki bulundu (p=0.009). Kadınlarla erkekler arasında TD açısından fark saptanmadı.

Sonuç: Araştırmamızda uzun süreli antipsikotik kullanımının TD ile ilişkisiz olduğu, yaşın ise TD riski açısından önemli bir etken olduğu saptanmıştır. Birinci kuşak antipsikotik tedaviden ikinci kuşağa geçmesinin ise TD sıklığını azaltmadığı söylenebilir.

Anahtar kelimeler: Antipsikotik, mental retardasyon, tardiv diskinezi

Address reprint requests to / Yazışma adresi:
Aylin Can,
Bakirkoy Training and Research Hospital for Psychiatry, Neurology and Neurosurgery, Zuhuratbaba Mah. Dr. Tevfik Saglam Cad. No: 25/2, 34147, Bakirkoy/Istanbul, Turkey

Phone / Telefon: +90-212-409-1515

E-mail address / Elektronik posta adresi: canaylin@gmail.com

Date of receipt / Geliş tarihi:
April 12, 2015 / 12 Nisan 2015

Date of the first revision letter / İlk düzeltme öneri tarihi:
February 18, 2015 / 18 Şubat 2015

Date of acceptance / Kabul tarihi:
May 28, 2015 / 28 Mayıs 2015

INTRODUCTION

Tardive dyskinesia (TD) is an iatrogenic movement disorder, related to long-term use of dopamine receptor blocking agents, characterized by stereotyped choreiform or athetoid involuntary movements affecting particularly mouth, tongue, and face, but occasionally also observed in the limbs and the trunk (1,2). It occurs after uninterrupted use of dopamine blockers for at least 3 months (3). The movement disorder has to be related temporally to the exposure to at least one antipsychotic drug (at least 3 months; in persons of the age of 60 years and above one month) (DSM-IV), TD develops during exposure to a DRBA for at least 3 months (or 1 month in patients age 60 years or older) or within 4 weeks of withdrawal from an oral medication (or within 8 weeks of withdrawal from a depot medication) (2). TD shows an insidious onset, develops the clinical picture within days/weeks, and its symptoms tend to continue for years (4). Other than antipsychotics, also antiemetics, antidepressants, antiepileptics, anticholinergics, calcium channel blockers, sympathomimetics, and antiparkinson drugs can cause TD (4-6).

TD began to be seen after in the 1950s the first generation of antipsychotics came into use, and the first case was reported in 1957 (1,7,8). In 1964, Faurbye (9) observed the emergence of involuntary motoric movements in psychotic patients under long-term medication and defined these as TD. While it had been thought that first-generation antipsychotics involved a higher risk for TD, given their stronger and longer binding to the D2 receptor (10,11), some recent publications have shown that, contrary to these assumptions, the TD risk from second-generation antipsychotics is no different from that of first-generation drugs (12,13).

Long-term follow-up studies have shown a TD incidence of 5% in patients with psychotic disorders using first-generation antipsychotics, while this figure reached 25-30% in the elderly (14,15). A review by Yassa and Jeste (16) examining 76 published studies including patients with schizophrenia or mental retardation, however, reported a prevalence of 24%. Early-onset extrapyramidal side effects are an important and potentially modifiable risk factor (17). Among the other risk factors are advanced age (16,18), female sex (16,18,19), long-term drug use, use of first generation antipsychotics (20), presence of brain damage or cognitive disorder (21) or mood disorder, use of alcohol or psychoactive substances, diabetes mellitus, or being of African ethnicity (16,22-24). When reviewing the literature, we found that the common risk factors were advanced age and long-term drug use (4,21,17).

In Turkey, data regarding the incidence of TD and associated factors in mentally retarded patients is fairly limited. Worldwide, study populations consist of patients receiving treatment during long-term hospitalization. Considering that mentally retarded outpatients' compliance with medication is low, we can assume that it is worth studying movement disorders with inpatients receiving very long-term medication under the supervision of healthcare staff. In this sense, our study aims at establishing the incidence of TD and associated factors among long-term inpatients with mental retardation and comorbid schizophrenia or other psychotic disorders being treated on the chronic psychiatric wards. While it can be expected that long-term regular use of antipsychotics results in a high incidence of dyskinesia, we can expect that, given the control of some risk factors, the incidence of TD might not be higher than in the literature or even lower.

METHOD

This study was carried out with long-term patients hospitalized at the Bakirkoy Prof. Dr. Mazhar Osman Training and Research Hospital for Psychiatry Neurology and Neurosurgery receiving treatment and care on the chronic wards, because of weak social support, with a diagnosis of medium-level or severe mental retardation according to the Diagnostic and Statistical Manual (DSM IV-TR) who had been using an antipsychotic drug for at least 3 months. Of

a total of 70 patients those with general medical conditions preventing the administration of the scales or those at an advanced level where they could not conform to the examination instructions were excluded from the study. We planned to include 43 patients whose medical records we could access, but three patients did not have a history of antipsychotic treatment and were excluded; thus the study was completed with 40 patients. Our study was approved by the local ethics committee.

Data Collecting Instruments

After completing a self-designed sociodemographic data form based on patient records, we administered the following instruments:

Abnormal Involuntary Movements Scale (AIMS): Developed in 1976 by the American National Institute of Mental Health's Research Unit on Psychopharmacology, the AIMS allows for a detailed evaluation of dyskinesias occurring in patients receiving antipsychotic treatment. In consists of 12 items. The first 4 items assess facial and oral movements, items 5-7 extremity and trunk movements, items 8-10 the measured and self-reported severity of these involuntary movements, and items 11 and 12 record the dental and denture status (3). In our study, we used the Schooler and Kane (25) diagnostic criteria to evaluate TD, according to which TD is diagnosed if the patient has been under antipsychotic treatment for at least 3 months, the first seven AIMS items, assessing seven different regions of the body, record at least two scores of 2 (mild) or one score of 3 (moderate), and there is no other disease to account for the movement disorder more adequately.

Barnes Akathisia Rating Scale (BARS): This scale was developed in 1989 by Barnes in order to assess the degree of akathisia caused specifically by antipsychotics. It includes four subscales to evaluate objective and subjective awareness of akathisia, distress related to restlessness, and a global clinical assessment of akathisia. The first three of these subscales give scores between 0 and 3, the last one from 0-5. A patient scoring at least once 2 points was considered to meet the criteria for akathisia (26).

Simpson-Angus Scale (SAS): This scale, developed for the assessment of neuroleptic-induced movement disorders, consists of 10 items scored with 0-4 points (27). In the evaluation, the scores for all items are summed up and divided by 10. With a score of 0.3 and above, a diagnosis of neuroleptic-induced Parkinsonism is made (28).

Procedure

Reviewing the hospital files, patients' age, sex, smoking status, and the presence of chronic comorbities such as hypertension and diabetes mellitus were ascertained. It was determined what type of antipsychotic (first or second generation) patients were using during the research period and how long they had been using them for. They were further categorized according to which generation antipsychotic they had been using for the longest period. It was recorded if the participants had used any centrally acting anticholinergic agent in the past. The scales were administered by psychiatrists who were blinded to the drug use of the patients they assessed. The administrators had received training for standardization purposes.

Statistical Analysis

Participant data were analyzed using SPSS (Statistical Package for the Social Sciences) version 20. After descriptive statistics, categorical variables were processed with the Chi-square test, continuous variables in independent groups with t-test. In order to examine correlations between the continuous variables, correlation analyses were made. A value for $p<0.05$ was accepted as significant. For continuous variables that did not follow normal distribution, Mann-Whitney U was used.

RESULTS

Of the 40 patients included in the study, 30 (75%) were male, and the mean age of the sample was 51 (±13.9). None of the participants had received any formal training, and 12 (30%) were actively smoking during the period of our research.

In their histories of antipsychotics use, 21 patients (52.5%) had used first-generation antipsychotics (haloperidol, zuclopenthixol, flupenthixol, fluphenazine, pimozide, chlorpromazine, thioridazine) in the past and continued to do so, while 19 patients (47.5%) had moved on from a first-generation to a second-generation antipsychotic (risperidone, olanzapine, quetiapine, clozapine, sulpiride, amisulpride). It was found that all of patients had used anticholinergic treatment (biperidene) at least in one part of their treatment. Twenty nine patients (72.5%) had used first-generation antipsychotics for the longest period, while 11 patients (27.5%) had used second-generation drugs longer. The duration of use for the previously most long-term used antipsychotic agent was on average 184 months (min: 36, max: 480 months) (Table 1).

The patients' average AIMS score was 3.98 (±4.2). According to AIMS criteria, TD was found in 9 patients (22.5%). A correlation between the antipsychotic type used for the longest period and TD could not be found (p=0.686). Comparing patient histories between those who had been and still were using first-generation antipsychotics and those who had moved from first- to second-generation drugs, no significant difference regarding TD could be found (p=0.546). No significant correlation was found between the type of antipsychotic used for the longest period and AIMS scores (p=0.432; r=0.128).

Between the class and duration of antipsychotic treatment used for the longest time and the incidence of TD, no significant correlation was found (p=0.194). Between the presence of chronic comorbidities (hypertension or diabetes mellitus) or smoking and the presence of TD, a significant correlation was not seen (p=0.215). The average age in the group with TD was significantly higher than in the non-affected group, when analysed with Mann-Whitney U test (U=64.50, p=0.015).

Comparing sexes with chi-square test, no significant difference was found between women and men regarding TD (χ^2=0.048, p=0.665).

In the participants, the presence of comorbid drug-induced Parkinsonism and akathisia were assessed (Table 2). The patients' mean SAS score was 0.88 (±0.67), and according to these scores, 17 (42.5%) had drug-induced Parkinsonism. Between the duration of the previously most long-term used antipsychotic treatment and SAS scores, no significant correlation was found (p=0.215; r=0.200). In addition, no significant correlation was found between SAS scores and gender (p=0.111). According to the BARS scores, none of the participants had tardive akathisia.

When evaluating the patients for all tardive movement disorders, these were found in 23 patients (57.5%) (Table 2).

Table 1: Antipsychotic-use status of patients included in the study

	1. Generation Antipsychotic		2. Generation Antipsychotic	
	n	%	n	%
Currently used antipsychotic (n=40)	21	52.5	19	47.5
Most long-term used antipsychotic (n=40)	29	72.5	11	27.5

Table 2: Tardive dyskinesia among participants by gender

	Male (n=30)		Female (n=10)	
	n	%	n	%
Tardive dyskinesia	6	20	3	30
Tardive parkinsonism	15	50	2	20
Tardive movement disorder	18	60	5	50

DISCUSSION

Since their discovery in the 1950s, antipsychotic drugs have been used increasingly in persons with mental retardation accompanied by psychiatric and behavioral disorders (8). With the use of these drugs, in the long run tardive movement disorders began to be seen (4). Our study analyzed TD occurring in mentally retarded persons having used antipsychotic drugs regularly over an extended period under the control of the healthcare team. Two independent studies in the literature had found a TD rate of 34% in mentally retarded individuals using antipsychotics (21,29). In our study, we found TD in 22.5% of our participants. The fact that for many years these persons had been under the control of healthcare staff who early on could notice extrapyramidal side effects, especially TD risk factors, and adopt required measures, might account for the lower TD rate in our results. Another explanation for the low TD rates might be that all participating patients in the study were of Caucasian ethnicity.

In a review article analyzing the data of 2769 patients in 11 long-term follow-up studies, it was shown that the risk of developing TD was higher with the use of first- rather than with second-generation antipsychotics (17). However, this comparison was made with haloperidol, a potent first-generation antipsychotic. A meta-analysis by Leucht et al. (13) with 2320 patients did not find a difference for extrapyramidal side effects between less potent first-generation and second-generation antipsychotics except for clozapine. In a 4-year prospective cohort study with 352 patients from 2010, the risks of developing TD did not differ between users of first- and second-generation antipsychotics (30). Consistent with these data, our study, too, did not find any correlation between the risk of developing TD and the type of antipsychotic currently used of the type having been used for the longest period in the past. One limitation of our study is that all participants currently using a second-generation antipsychotic or having used a second-generation drug for the longest time during the past had at one time during their lives used a first-generation antipsychotic, and we did not know what type they had been using at the time when the TD symptoms set on. The small sample size may also have an effect of our study results. At least, we can say that our results do not show a marked difference, regarding TD, for the later transition from first- to second-generation antipsychotic use, and an inhibiting group effect has not been shown.

Several studies have shown that one of the most important factors increasing the risk for TD is advanced age (4,25). While in young persons an annual incidence of 3-5% is observed, it can reach 30% in individuals of advanced age. This increase might be explained by a cumulative increase of exposure to antipsychotic drugs (4). Sachdev's (21) study with mentally retarded persons also showed that the risk of TD increased with age. Equally, Cohen et al. (31) showed in a study with 60 mentally retarded participants that advanced age was a risk factor for TD. Consistent with the literature, our study also found that the rate of TD was increased with advanced age.

Regarding gender, studies show that the disposition for TD in both sexes is at the same level (4). However, the risk appears to be increased in postmenopausal women, which suggests a protective effect of estrogen (4). Our study did not find a significant difference for TD between female and male participants. This is in line with the study done with mentally retarded persons by Sachdev (21), who did not see an effect of gender on the development of TD.

When we evaluated our sample according to the antipsychotic type that individuals had been exposed to for the longest period during their therapy, we found this period to be almost 15 years, which is a fairly long time. It can be said that the duration of antipsychotic use and the increase of the total exposure dose might be a risk factor for TD. Even studies suggesting that second-generation antipsychotics present a low risk for TD point out that with an increase in the dose of the antipsychotic used, the risk also rises (4). By contrast, a study by Cohen et al. (31) showed that the duration of antipsychotic use was not related with TD. Similarly, our study also did not find a correlation between the duration of antipsychotic use and an onset of TD. However, to assess these risk factors more adequately,

prospective studies need to be made. Another limitation of our study is the lack of data about the duration of antipsychotic use in some patients before being admitted to hospital. Since the total dose of antipsychotics used in our sample is not known to us, we cannot evaluate the cumulative dose effect.

In conclusion, while it can be debated how representative our study, carried out in a fairly specific group, is for mentally retarded patients with comorbid schizophrenia or other psychotic disorders in Turkey, we can say that we have obtained useful information reflecting a patient group that was guaranteed regular drug use, which is one of the greatest problems in this type of patients. Further research is needed to evaluate the prevalence of TD in Turkey, which is still one of the most important problems, considering the complexity of pathogenesis, difficulty of treatment, and the burden involved.

Contribution Categories	Name of Author
Development of study idea	A.C., A.N., H.S.B., A.C., K.F.Y., M.A.D., E.K.
Methodological design of the study	A.C., A.N., H.S.B., A.C., K.F.Y., M.A.D., E.K.
Data acquisition and process	A.C., A.N., H.S.B., A.C.,
Data analysis and interpretation	A.C., A.N., H.S.B., A.C., K.F.Y., M.A.D., E.K.
Literature review	A.C., A.N., H.S.B., A.C., K.F.Y.
Manuscript writing	A.C., A.N., H.S.B., A.C., K.F.Y., M.A.D., E.K.
Manuscript review and revisation	A.C., A.N., H.S.B., A.C., K.F.Y., M.A.D., E.K.

Conflict of Interest: Authors declared no conflict of Interest.

Financial Disclosure: Authors declared no financial support.

REFERENCES

1. Schonecker M. Paroxysmal dyskinesia as the effect of megaphen. Nervenarzt 1957; 28:550-553. (German)
2. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. Fourth ed., Text Revision (DSM-IV TR). Washington, DC: American Psychiatric Association; 2000.
3. Guy W. Abnormal Involuntary Movement Scale (AIMS). ECDEU Assessment Manual for Psychopharmacology Revised. Rockville (MD): Alcohol, Drug Abuse, and Mental Health Administration, National Institute of Mental Health, 1976; 534-537.
4. Waln O, Jankovic J. An update on tardive dyskinesia: from phenomenology to treatment. Tremor Other Hyperkinet Mov (NY) 2013; 12:3.
5. Albayrak Y, Ekinci O. Duloxetine-associated tardive dyskinesia resolved with fluvoxamine: a case report. J Clin Psychopharmacol 2012; 32:723-724. **[CrossRef]**
6. Birthi P, Walters C, Karandikar N. A rare case of tardive dyskinesia and akathisia induced by citalopram. PM R 2010; 2:973-975. **[CrossRef]**
7. Fernandez HH, Friedman JH. Classification and treatment of tardive syndromes. Neurologist 2003; 9:16-27. **[CrossRef]**
8. Advokat CD, Mayville EA, Matson JL. Side effect profiles of atypical antipsychotics, typical antipsychotics, or no psychotropic medications in persons with mental retardation. Res Dev Disabil 2000; 21:75-84. **[CrossRef]**
9. Faurbye A, Rasch PJ, Petersen PB, Brandborg G, Pakkenberg H. Neurological symptoms in pharmacotherapy of psychoses. Acta Psychiatr Scand 1964; 40:10-27. **[CrossRef]**
10. Gharabawi GM, Bossie CA, Zhu Y. New-onset tardive dyskinesia in patients with first-episode psychosis receiving risperidone or haloperidol. Am J Psychiatry 2006; 163:938-939. **[CrossRef]**
11. Eberhard J, Lindstrom E, Levander S. Tardive dyskinesia and antipsychotics: a 5-year longitudinal study of frequency, correlates and course. Int Clin Psychopharmacol 2006; 21:35-42. **[CrossRef]**
12. Hugenholtz GW, Heerdink ER, Stolker JJ, Meijer WE, Egberts AC, Nolen WA. Haloperidol dose when used as active comparator in randomized controlled trials with atypical antipsychotics in schizophrenia: comparison with officially recommended doses. J Clin Psychiatry 2006; 67:897-903. **[CrossRef]**
13. Leucht S, Wahlenbeck K, Hamann J, Kissling W. New generation antipsychotics versus low-potency conventional antipsychotics: a systematic review and meta-analysis. Lancet 2003; 361:1581-1589. **[CrossRef]**
14. Glazer WM, Morgenstern H, Doucette JT. Predicting the long-term risk of tardive dyskinesia in outpatients maintained on neuroleptic medications. J Clin Psychiatry 1993; 54:133-139.
15. Jeste DV, Lacro JP, Palmer B, Rockwell E, Harris MJ, Caligiuri MP. Incidence of tardive dyskinesia in early stages of low-dose treatment with typical neuroleptics in older patients. Am J Psychiatry 1999; 156:309-311.

16. Yassa R, Jeste DV. Gender differences in tardive dyskinesia: a critical review of the literature. Schizophr Bull 1992; 18:701-715. **[CrossRef]**

17. Correll CU, Leucht S, Kane JM. Lower risk for tardive dyskinesia associated with second-generation antipsychotics: a systematic review of 1-year studies. Am J Psychiatry 2004; 161:414-425. **[CrossRef]**

18. Stone RK, May JE. Alvarez WF, Ellman G. Prevalence of dyskinesia and related movement disorders in a developmentally disabled population. J Ment Defic Res 1989; 33:41-53. **[CrossRef]**

19. Rao JM, Cowie VA. Mathew B. Tardive dyskinesia in neuroleptic medicated mentally handicapped subjects. Acta Psychiatr Scand 1987; 76:507-513. **[CrossRef]**

20. Chong SA, Sachdev PS. The Epidemiology of Tardive Dyskinesia. In Sethi KD (editor). Drug-Induced Movement Disorders. First ed., New York: Marcel Dekker Inc, 2004; 37-60.

21. Sachdev P. Drug-induced movement disorders in institutionalised adults with mental retardation: clinical characteristics and risk factors. Aust N Z J Psychiatry 1992; 26:242-248. **[CrossRef]**

22. Tarsy D, Baldessarini RJ. Epidemiology of tardive dyskinesia: is risk declining with modern antipsychotics? Mov Disord 2006; 21:589-598. **[CrossRef]**

23. Bhidayasiri R, Boonyawairoj S. Spectrum of tardive syndromes: clinical recognition and management. Postgrad Med J 2011; 87:132-141. **[CrossRef]**

24. Tan CH, Tay LK. Tardive dyskinesia in elderly psychiatric patients in Singapore. Aust N Z J Psychiatry 1991; 25:119-122. **[CrossRef]**

25. Schooler NR, Kane JM. Research diagnoses for tardive dyskinesia. Arch Gen Psychiatry 1982; 39:486-487. **[CrossRef]**

26. Barnes TR. A rating scale for drug-induced akathisia. Br J Psychiatry 1989; 154: 672-676. **[CrossRef]**

27. Simpson GM, Angus JWS. A rating scale for extrapyramidal side effects. Acta Psychiatr Scand 1970; 212:11-19. **[CrossRef]**

28. Janno S, Holi MM, Tuisku K, Wahlbeck K. Validity of Simpson-Angus Scale (SAS) in a naturalistic schizophrenia population. BMC Neurol 2005; 5:5. **[CrossRef]**

29. Gualtieri CT, Schroeder SR, Hicks RE, Quade D. Tardive dyskinesia in young mentally retarded individuals. Arch Gen Psychiatry 1986; 43:335-340. **[CrossRef]**

30. Woods SW, Morgenstern H, Saska JR, Walsh BC, Sullivan MC, Money R, Hawkins KA, Gueorguieva RV, Glazer WM. Incidence of tardive dyskinesia with atypical and versus conventional antipsychotic medications: prospective cohort study. J Clin Psychiatry 2010; 71:463-474. **[CrossRef]**

31. Cohen S, Khan A, Zheng Y, Chiles J. Tardive dyskinesia in the mentally retarded: comparison of prevalence, risk factors and topography with a schizophrenic population. Acta Psychiatr Scand 1991; 83:234-237. **[CrossRef]**