Review of Incidence Studies of Tardive Dyskinesia Associated With Typical Antipsychotics

William M. Glazer, M.D.

Unless researchers make an organized effort, patients with tardive dyskinesia are difficult to study and easily lost to follow up. Because there is no treatment for tardive dyskinesia, investigators are obliged to study the natural history of the disorder and identify risk and prognostic factors to further understand pathophysiologic mechanisms and to guide prevention and treatment efforts. Abundant variability exists among incidence studies of tardive dyskinesia, depending to some extent on design issues. In this article, the design concepts of incidence and prevalence studies are described, along with results, methodological problems, and identified risk factors in various tardive dyskinesia incidence studies involving the use of typical antipsychotic medications.

(J Clin Psychiatry 2000;61[suppl 4]:15–20)

Unless researchers make an organized effort, patients with tardive dyskinesia are difficult to study and easily lost to follow up. Because there is no treatment for tardive dyskinesia, investigators are obliged to study the natural history of the disorder and identify risk and prognostic factors to further understand pathophysiologic mechanisms and to guide prevention and treatment efforts. In this article, design concepts of incidence and prevalence studies are described, along with results, methodological problems, and identified risk factors in various tardive dyskinesia incidence studies involving the use of typical antipsychotic medications.

Several important methodological problems may occur with published research. The use of prevalence comparisons fails to distinguish between risk factors and prognostic factors, which is a most important issue for controlling disease. Additionally, many etiologic investigations have been cross-sectional rather than longitudinal in nature, and cross-sectional studies of patient populations are particularly vulnerable to selection biases and temporal ambiguities of cause and effect. Moreover, statistical analyses used in some published studies are often simplistic and occasionally inappropriate. Most relevant in this regard is the relative lack of multivariable methods. For example, some investigators fail to consider potential confounders, effect modifiers, or intervening variables.

Another methodological research problem is the clinical assessment that causes difficulty in the diagnosis and classification of tardive dyskinesia and makes it difficult to use any convenient psychiatric population to test hypotheses. Two types of rating scales—multiple-item scales and global judgment scales—are primarily used for quantifying symptom severity. The reliability and validity of these measuring instruments are sometimes questionable and the relationship between scales is poorly understood. In addition, the diagnostic custom of identifying cases of tardive dyskinesia generally depends on a knowledge of possible etiologic factors such as the use of typical antipsychotic (neuroleptic) medications. The differential diagnosis of tardive dyskinesia is complex and—as suggested by empirical and biological data—multiple syndromes may cause abnormal movements that are collectively referred to as tardive dyskinesia. Each of the syndromes may have a different etiology, so that the determinants of one syndrome may not be the determinant of another syndrome.

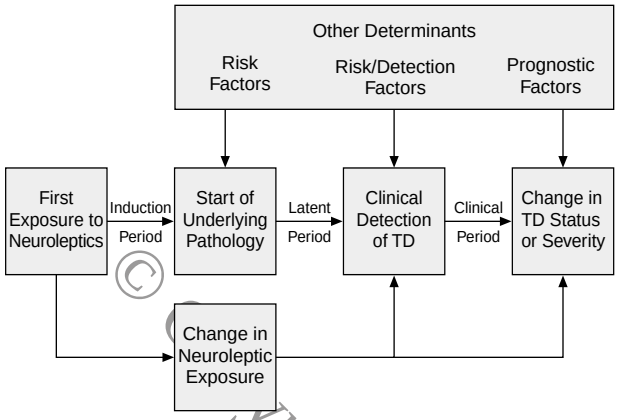
Another factor that contributes to diagnostic and classification difficulties is the considerable variability among patients of abnormal movements over time. It is quite possible that patients who demonstrate exacerbation or masking of existing abnormal movements following reduction or increase of medication dosage are etiologically or pathophysiologically distinct from patients whose movements do not follow such patterns following similar drug changes. Thus far, researchers have little notion of the factors that lead to improvement or worsening of tardive dyskinesia severity in the longitudinal course of the disorder. Furthermore, investigators are unsure of the degree to which the variability of movements over time is due to measurement difficulties (reliability) or to the disease itself (stability). With all of this uncertainty, it is important

From the Harvard Medical School, Massachusetts General Hospital, Boston.

Presented at the symposium "Update on Tardive Dyskinesia," which was held March 23, 1999, Dallas, Tex., and supported by an unrestricted educational grant from Eli Lilly and Company.

Reprint requests to: William M. Glazer, M.D., P.O. Box 121, Menemsha, MA 02552.

Figure 1. The Natural History of Tardive Dyskinesia[a]



[a]Reprinted from Glazer and Morgenstern,[3] with permission.
Abbreviation: TD = tardive dyskinesia.

to understand what the risk factors for tardive dyskinesia are. Without such knowledge, it will be close to impossible to ever identify the etiologic mechanisms underlying the disorders.

A concept of the different stages of the natural history of tardive dyskinesia was used in the Yale Tardive Dyskinesia Study[1,2] that researched the incidence of tardive dyskinesia and associated risk factors (Figure 1).[3] In that conceptual framework, the natural history of tardive dyskinesia consists of an induction period, a latent period, and a clinical period. When a patient is first exposed to neuroleptics, the induction period begins and leads to the start of underlying brain pathology. Various risk factors contribute to the emergence of the underlying pathology. The subsequent latent period is followed by clinical detection of tardive dyskinesia. Once tardive dyskinesia has been identified, changes in status or severity are noted. Risk factors are those factors that contribute to the development of tardive dyskinesia from the first exposure to neuroleptics to the beginning of underlying pathology. Prognostic factors affect the course of tardive dyskinesia once it has emerged.

Gardos and Cole[4] point out the importance of conducting incidence studies in a wide range of population at risk over a long period of time to obtain an understanding of the extent to which tardive dyskinesia poses a public health concern. Many clinicians have difficulty understanding the incidence design and its implications. By definition, the incidence design always starts with noncases; one does not have to have a disease to enter an incidence study. With proper measurements, cases of the disease emerge over time, and the comparison between cases and noncases leads to identification of the risk factors. An incidence design can accurately identify risk factors, although prevalence studies also help to point the way toward identifying risk factors. A prevalence design is usually not longitudinal; that is, it is a measurement of cases and noncases taken together at one point in time.

Abundant variability exists among incidence studies of tardive dyskinesia, depending to some extent on design issues. Some studies look at patients who are slightly or newly exposed to neuroleptics; other studies follow a population of chronically exposed patients. Although most patients with tardive dyskinesia have a psychiatric diagnosis of schizophrenia, a combination of populations should ideally be assessed to provide the maximum data. The frequency of patient assessments over time is another important design issue, along with the length of the follow-up period. Many studies perform a baseline assessment with a follow-up assessment 5 or 10 years later, which provides only a 2-point measurement; other studies provide multiple examinations over a long period of time. Other design issues are the consideration of a prior history of tardive dyskinesia at baseline, the number of observations used to exclude tardive dyskinesia at baseline, and the number of positive observations required to diagnose incident cases of tardive dyskinesia.

SOURCES OF VARIABILITY IN INCIDENCE STUDIES

The patient population, methodology, and results of previous tardive dyskinesia incidence studies are reviewed in the following tables. The study populations are summarized in Table 1.[1,2,5–18] Most patients had a psychiatric diagnosis of schizophrenia, but several studies also included patients with a diagnosis of schizoaffective disorder, and some studies included patients with a diagnosis of mood disorder. Other diagnoses included mental retardation, organic mental disorders, and mixed or unspecified diagnoses. Gardos and colleagues[11] did not report patient diagnoses. Study populations differed with respect to a wide variability in past neuroleptic exposure with mean or median exposure ranging from 0.6 weeks to 20 years. Studies also varied between age focus—that is, geriatric (greater than age 65 years) versus nongeriatric populations. This variability might be expected to have an impact on the observed incidence of tardive dyskinesia in the studies.

The methods used to diagnose incident cases of tardive dyskinesia are summarized in Table 2.[1,2,5–18] Two points of distinction in these incidence analyses are whether patients with a prior history of tardive dyskinesia were systematically excluded and how extensively patients were assessed for tardive dyskinesia at baseline. Although all of these studies (by definition) excluded patients with tardive dyskinesia at baseline, most studies employed only 1 baseline assessment to evaluate a patient's tardive dyskinesia status. However, the Yale Group[1,2] published a second analysis of incidence data in which 2 assessments (baseline and first postbaseline visit) were used to establish a patient's tardive dyskinesia status. Patients included in this

Table 1. Comparison of Tardive Dyskinesia Incidence Studies: Study Population

Study	N	Mean Age (y)	Male (%)	Neuroleptic Exposure at Baseline (y)	All Patients on Neuroleptics at Baseline?	Psychiatric Diagnosis
Gibson (1981)[5]	342	≅ 50[a]	≅ 30[a]	≅ 11.1[a,b]	Yes	Schizophrenia
Kane et al (1982, 1984)[6,7]	421	≅ 28[a]	≅ 54[a]	≅ 10 mo[a,c]	No	Schizophrenia, schizoaffective disorder, mood disorder
Yassa and Nair (1984)[8]	108	48	51	17.6[b]	Yes	Schizophrenia, mood disorder, mental retardation, organic mental disorder
Chouinard et al (1986,1988)[9,10]	131	40[c]	47	9.5[c]	Yes	Schizophrenia
Gardos et al (1988)[11]	51	44[a]	41	≅ 14[a,b]	Yes	Not reported
Waddington et al (1990)[12]	38	56	58	16[b]	Yes	Schizophrenia
Inada et al (1991)[13]	1012	50	56	20[b]	No	Schizophrenia, mood disorder, mental retardation
Glazer et al (1993)[1]	362	41[c]	47	6.1[c]	Yes	Schizophrenia, schizoaffective disorder, mood disorder, other
Morgenstern and Glazer (1993)[2]	340	≅ 41[a,c]	≅ 47[a]	6.1	Yes	Schizophrenia, schizoaffective disorder, mood disorder, other
Chakos et al (1996)[14]	117	≅ 25[a]	≅ 52[a]	≅ 0.6 wk[a,b]	No	Schizophrenia
Geriatric studies						
Woerner et al (1998)[15]	261	77	69	None	No	Organic mental syndromes, major mood disorder, schizophrenia or schizoaffective disorder, anxiety/other disorder
UCSD group[d]						
Paulsen et al (1996)[16]	266	66	81	21 d[c]	No	Dementia, schizophrenia, mood disorder, organic/nonorganic disease
Caligiuri et al (1997)[17]	378	65	79	39 d[b]	No	Organic mental syndromes, schizophrenia, mood disorder, mixed diagnoses
Jeste et al (1999)[18]	307	66	81	≤ 5	No	Dementia, schizophrenia, schizoaffective disorder, organic psychoses, mood disorder

[a]Data regarding patient age, sex distribution, and baseline neuroleptic exposure were estimated from the published results and are cited as approximate values.
[b]Mean.
[c]Median.
[d]These 3 studies had overlapping populations. Abbreviation: UCSD = University of California, San Diego.

particular analysis could meet the criteria for tardive dyskinesia at baseline as long as they failed to meet the criteria at the first postbaseline assessment. None of these studies required a patient's failure to meet diagnostic criteria for tardive dyskinesia at multiple baseline evaluations before inclusion in the incidence analysis.

A third point of distinction concerns the criteria used to determine the presence of tardive dyskinesia. Most incidence studies have used the Abnormal Involuntary Movement Scale (AIMS) to measure the severity of tardive dyskinesia; however, the AIMS examination alone is not diagnostic of tardive dyskinesia. Two diagnostic systems for tardive dyskinesia that rely on the AIMS scores have emerged: the Schooler-Kane[19] system and the Glazer-Morgenstern[2] system. The Schooler-Kane criteria require a sum of 4—that is, a score of ≥ 3 on any 1 of the AIMS categorical items 1 through 7 and ≥ 1 on another of the categorical items, or ≥ 2 on any 2 of the categorical items. The Glazer-Morgenstern criteria require a sum of 3 on AIMS categorical items—that is, a score of ≥ 3 on any 1 of AIMS categorical items 1 through 7, or ≥ 2 on 1 of the categorical items and ≥ 1 on another of the categorical items. Investigators in the Yale Group have observed that patients who meet the criteria for tardive dyskinesia by the Glazer-Morgenstern criteria eventually meet the more stringent Schooler-Kane criteria (Glazer WM, Morgenstern H, unpublished data, 1987). Thus, the Glazer-Morgenstern criteria could serve as a screening tool to use at baseline to avoid false negative cases, while the Schooler-Kane criteria are more suitable for the identification of incidence cases when one wants to avoid false positive cases.

Another factor that influenced the diagnosis of tardive dyskinesia was the number of observations required to make a positive diagnosis. The studies by Yassa and Nair,[8] the Yale Group,[1,2] Woerner et al.,[15] and the University of California, San Diego group[16–18] required diagnostic criteria to be met for 2 consecutive visits for a diagnosis of tardive dyskinesia. The remaining studies required diagnostic criteria to be met at only 1 visit for a diagnosis of tardive dyskinesia. A final methodologic issue concerns the duration and frequency of patient observation. In these studies, the frequency of patient assessment ranges from 8 weeks in the Chakos et al. study[14] to several years in other studies.

The risk of tardive dyskinesia among geriatric patients is higher, as the table shows. A longer study duration and more frequent assessments will increase the accuracy of the found incidence of tardive dyskinesia.

Despite the wide variability in patient populations and case assessment methods used across these incidence studies, the results of the assessments are similar in the nongeriatric adult populations, with estimated annual risks of

Table 2. Comparison of Tardive Dyskinesia Incidence Studies: Methodology*

Study	Length of Follow-Up (y)	Frequency of Assessment	Diagnostic Criteria	Prior History of TD Considered to Exclude TD at Baseline	Observations (N) Considered to Exclude TD at Baseline	Positive Observations (N) to Diagnose Incident TD
Gibson (1981)[5]	3	1/y	At least mild dyskinetic movement by author's examination	No	1	1
Kane et al (1982, 1984)[6,7]	Up to 7	4/y	$AIMS_{(1–7)}$ 1 item ≥ 3 or (1 item ≥ 2 and 1 item ≥ 2)	No	1	1
Yassa and Nair (1984)[8]	2	3/y	$AIMS_{(1–7)}$ 1 item ≥ 2	Yes	1	2
Chouinard et al (1986, 1988)[9,10]	5	Endpoint	$AIMS_{(1–7)}$ 1 item ≥ 3 or (1 item ≥ 2 and 1 item ≥ 2)	No	1	1
Gardos et al (1988)[11]	7	Endpoint	$AIMS_{(1–7)}$ 1 item ≥ 3 or (1 item ≥ 2 and 1 item ≥ 2)	No	1	1
Waddington et al (1990)[12]	5	Endpoint	$AIMS_{(1–7)}$ 1 item score ≥ 2	No	1	1
Inada et al (1991)[13]	1	Endpoint	$AIMS_{(1–7)}$ total score > 2	No	1	1
Glazer et al (1993)[1]	5	2/y	$AIMS_{(1–7)}$ 1 item ≥ 3 or (1 item ≥ 2 and 1 item ≥ 1)	Yes	2	2
Morgenstern and Glazer (1993)[2]	5	2/y	$AIMS_{(1–7)}$ 1 item ≥ 3 or (1 item ≥ 2 and 1 item ≥ 1)	Yes	1	2
Chakos et al (1996)[14]	Up to 8.5	q 8 wk	Simpson Dyskinesia Scale Global score ≥ 2	NA[a]	1	Presumptive TD (1) Persistent TD (2)
Geriatric studies						
Woerner et al (1998)[15]	3–393 wk	4/y	Tardive Dyskinesia Scale, $AIMS_{(1–7)}$, Simpson-Angus Scale	NA[a]	1	2
UCSD group[b]						
Paulsen et al (1996)[16]	2	4/y	AIMS, Instrumental motor assessment, Simpson-Angus Scale, Simpson Abbreviated Dyskinesia Rating Scale	Yes	1	1
Caligiuri et al (1997)[17]	3	4/y	AIMS, Simpson-Angus Scale, Instrumental motor assessment	Yes	1	2
Jeste et al (1999)[18]	1	4/y	AIMS, Simpson-Angus Scale	Yes	1	1

*Abbreviations: AIMS = Abnormal Involuntary Movement Scale, TD = tardive dyskinesia.
[a]Only neuroleptic-naive patients were included in this study.
[b]These 3 studies had overlapping populations.

tardive dyskinesia ranging approximately between 4% and 8% per year (Table 3).[1,2,5–18] In the treatment of psychosis, greater overall benefit may be derived from using antipsychotics that carry less risk of causing movement disorders.

RISK FACTORS

Several risk factors have been identified as predictors of tardive dyskinesia in incidence studies involving the use of typical antipsychotic medications. These risk factors include age, gender, race, diagnoses of mood disorders or cognitive difficulties (including handedness), presence of negative symptoms, alcohol and substance abuse, antipsychotic treatment variables (type, dose, drug holidays, and targeted strategies), use of antiparkinsonian agents and lithium, early extrapyramidal symptoms (EPS), illness awareness, and diabetes. Most investigators agree that age is a risk factor for tardive dyskinesia, but the inclusion of gender as a risk factor may be misleading. A recent review[20] indicated that a number of prevalence studies have suggested that female gender is a risk factor for tardive dyskinesia. But incidence studies have not supported this finding, and this variance may be an example of the confusion between prognostic and risk factors. One possible explanation could be that some patients with severe cases of tardive dyskinesia are confined to state hospitals and are unable to be included in research studies whereas other patients may have a less severe disorder and can be followed by researchers in outpatient clinics. The Yale Tardive Dyskinesia Study[1,2] found that African-American patients were twice as likely to develop tardive dyskinesia than Caucasian patients, which suggests that race may be a risk factor. Jeste et al.[21] also indicated African-American race as a risk factor. This finding needs additional study.

Antipsychotic medication treatment variables include the type and dose of drug, intermittent drug exposure, and drug holidays. However, given methodological limitations, it can be difficult to predict changes in tardive dyskinesia incidence solely as a function of change in antipsychotic dosage. It is clear that the lower the antipsychotic drug dose the less risk for tardive dyskinesia, but data are scarce on the difference between high-potency and low-potency typical antipsychotics in relation to tardive dyskinesia incidence.

Early EPS

The suggestion that early EPS might be a predictor for development of tardive dyskinesia in patients treated with

Table 3. Comparison of Tardive Dyskinesia Incidence Studies: Results*

Study	Patient Years	Estimated Risk (%) 1 y	2 y	5 y
Gibson (1981)[5]	≅ 5.4[a]	…	…	…
Kane et al (1982, 1984)[6,7]	…	≅ 2	≅ 7	≅ 17
Yassa and Nair (1984)[8]	3.7	…	…	…
Chouinard et al (1986, 1988)[9,10]	7.02	8.4	…	…
Gardos et al (1988)[11]	5.32	…	…	…
Waddington et al (1990)[12]	8.42	…	…	…
Inada et al (1991)[13]	3.75	…	…	…
Glazer et al (1993)[1]	5.3	9.2	15.8	19.8
Morgenstern and Glazer (1993)[2]	4.7	…	…	…
Chakos et al (1996)[14]	…	6.3 presumptive 4.8 persistent	11.5 presumptive 7.2 persistent	17.5 presumptive (4 y) 15.6 persistent (4 y)
Geriatric studies				
Woerner et al (1998)[15]	…	25	34	53 (3 y)
UCSD group[b]				
Paulsen et al (1996)[16]	…	38.5 (orofacial) 18.6 (limbtruncal)	65.7 (orofacial) 32.6 (limbtruncal)	…
Caligiuri et al (1997)[17]	…	2.5	12.1	22.9 (3 y)
Jeste et al (1999)[18]	…	34.1 (< 60 years of age) 27.1 (≥ 60 years of age)	… …	… …

*Symbol: … = information missing.
[a]This figure was calculated from the published results of the study and was not reported by the author.
[b]These 3 studies had overlapping populations.

typical antipsychotics dates back to the 1970s.[22] The question of whether the risk for tardive dyskinesia is related to EPS or to the use of anticholinergic drugs has remained. Studies of both newly exposed patients and chronically exposed patients have been conducted to determine if early EPS is a predictor of tardive dyskinesia. Moreover, studies of both geriatric and nongeriatric populations have been conducted. Studies of geriatric patients are useful for investigating the incidence of tardive dyskinesia relative to EPS, because in a short period of time the incidence of tardive dyskinesia is higher in geriatric patients than in younger patients.

Kane et al.[23] compared the incidence of tardive dyskinesia in patients with no EPS to the incidence in patients with severe EPS. A survival analysis showed that patients who had EPS developed tardive dyskinesia to a greater degree than patients without EPS. The Woerner et al. study[15] examined 261 neuroleptic-naive patients aged 55 years and older. The investigators found that after 1, 2, and 3 years of cumulative typical neuroleptic treatment, the cumulative rates of tardive dyskinesia were 25%, 34%, and 53%. A greater risk of tardive dyskinesia was associated with the presence of EPS early in treatment. The authors recommended that alternative treatments be investigated.

To determine the incidence and risk factors for tardive dyskinesia in patients 45 years and older, Jeste et al.[21] evaluated 266 newly exposed patients treated with low- or high-potency typical antipsychotic agents. In an effort to overcome some of the problems associated with subjective ratings of EPS and improve early detection of EPS, a battery of instrumental assessment procedures were used, and an early tremor on instrumental assessment predicted tardive dyskinesia incidents. Other risk factors included the duration of prior antipsychotic use at baseline, cumulative amounts of high-potency typical antipsychotics, a history of alcohol abuse or dependence, and borderline or minimal dyskinesia.

A study with contrasting findings by Chatterjee et al.[24] assessed the prevalence of EPS and spontaneous dyskinesia in 89 neuroleptic-naive, first-break schizophrenia patients. Fifteen patients (16.9%) had EPS but only 1 patient had spontaneous dyskinesia at baseline. The authors found that there was no difference between patients with and without spontaneous EPS in terms of the subsequent development of persistent tardive dyskinesia. Thus, a majority of studies show a prospective relationship between EPS and tardive dyskinesia, which suggests that early EPS in the course of typical antipsychotic treatment is predictive of tardive dyskinesia.

CONCLUSION

Our knowledge of tardive dyskinesia is in its early phase, and longitudinal research is necessary if we are to understand this perplexing disorder. It is important to conduct incidence studies in a wide range of population at risk over a long period of time to obtain an understanding of the extent to which tardive dyskinesia poses a public health concern. Risk factors, such as age and early EPS, are those factors that contribute to the development of tar-

dive dyskinesia from the first neuroleptic exposure to the beginning of underlying pathology. An incidence design is necessary for a study to accurately identify risk factors for tardive dyskinesia that are associated with typical antipsychotic treatment.

Disclosure of off-label usage: The author has determined that, to the best of his knowledge, no investigational information about pharmaceutical agents has been presented in this article that is outside U.S. Food and Drug Administration–approved labeling.

REFERENCES

1. 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
2. Morgenstern H, Glazer WM. Identifying risk factors for tardive dyskinesia among long-term outpatients maintained with neuroleptic medications: results of the Yale Tardive Dyskinesia Study. Arch Gen Psychiatry 1993;50: 723–733
3. Glazer W, Morgenstern H. Predictors of occurrence, severity and course of tardive dyskinesia in an outpatient population. J Clin Psychopharmacol 1988;8(4, suppl):10S–16S
4. Gardos G, Cole JO. Overview: public health issues in tardive dyskinesia. Am J Psychiatry 1980;137:776–781
5. Gibson AC. Incidence of tardive dyskinesia in patients receiving depot neuroleptic injection. Acta Psychiatr Scand 1981;63:111–116
6. Kane JM, Woerner M, Weinhold P, et al. A prospective study of tardive dyskinesia development: preliminary results. J Clin Psychopharmacol 1982;2: 345–349
7. Kane JM, Woerner M, Weinhold P, et al. Incidence of tardive dyskinesia: five-year data from a prospective study. Psychopharmacol Bull 1984;20: 387–389
8. Yassa R, Nair V. Incidence of tardive dyskinesia in an outpatient population. Psychosomatics 1984;25:479–481
9. Chouinard G, Annable L, Mercier P, et al. A five-year follow-up study of tardive dyskinesia. Psychopharmacol Bull 1986;22:259–263
10. Chouinard G, Annable L, Ross-Chouinard A, et al. A 5-year prospective longitudinal study of tardive dyskinesia: factors predicting appearance of new cases. J Clin Psychopharmacol 1988;8(4, suppl):21S–26S
11. Gardos G, Perenyi A, Cole JO, et al. Seven-year follow-up of tardive dyskinesia in Hungarian outpatients. Neuropsychopharmacology 1988;1: 169–172
12. Waddington JL, Youssef HA, Kinsella A. Cognitive dysfunction in schizophrenia followed up over 5 years, and its longitudinal relationship to the emergence of tardive dyskinesia. Psychol Med 1990;20:835–842
13. Inada T, Ohnishi K, Kamisada M, et al. A prospective study of tardive dyskinesia in Japan. Eur Arch Psychiatry Clin Neurosci 1991;240:250–254
14. Chakos MH, Alvir JMJ, Woerner MG, et al. Incidence and correlates of tardive dyskinesia in first episode of schizophrenia. Arch Gen Psychiatry 1996;53:313–319
15. Woerner MG, Alvir JMJ, Saltz BL, et al. Prospective study of tardive dyskinesia in the elderly: rates and risk factors. Am J Psychiatry 1998;155: 1521–1528
16. Paulsen JS, Caligiuri MP, Palmer B, et al. Risk factors for orofacial and limbtruncal tardive dyskinesia in older patients: a prospective longitudinal study. Psychopharmacology 1996;123:307–314
17. Caligiuri MP, Lacro JP, Rockwell E, et al. Incidence and risk factors for severe tardive dyskinesia in older patients. Br J Psychiatry 1997;171: 148–153
18. Jeste DV, Lacro JP, Palmer B, et al. Incidence of tardive dyskinesia in early stages of low-dose treatment with typical neuroleptics in older patients. Am J Psychiatry 1999;156:309–311
19. Schooler NR, Kane JM. Research diagnoses for tardive dyskinesia [letter]. Arch Gen Psychiatry 1982;39:486–487
20. Yassa R, Jeste DV. Gender as a factor in the development of tardive dyskinesia. In: Yassa R, Nair NPV, Jeste DV, eds. Neuroleptic-Induced Movement Disorders. New York, NY: Cambridge University Press; 1997: 26–40
21. Jeste DV, Caligiuri MP, Paulsen JS, et al. Risk of tardive dyskinesia in older patients: a prospective longitudinal study of 266 patients. Arch Gen Psychiatry 1995;52:756–765
22. Crane GE. Pseudoparkinsonism and tardive dyskinesia. Arch Neurol 1972;27:426–430
23. Kane JM, Woerner M, Borenstein M, et al. Integrating incidence and prevalence of tardive dyskinesia. Psychopharmacol Bull 1986;22:254–258
24. Chatterjee A, Chakos M, Koreen A, et al. Prevalence and clinical correlates of extrapyramidal signs and spontaneous dyskinesia in never-medicated schizophrenic patients. Am J Psychiatry 1995;152:1724–1729