

Tardive Dyskinesia: A Task Force Report of the American Psychiatric Association

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ment of tardive dyskinesia are also risk factors for the persistence of tardive dyskinesia, as appears to be the case for advancing age. This should not be assumed to be true without appropriate data, but if it were true, this would serve to exaggerate the influence of a particular risk factor. For example, if both the incidence and the likelihood of persistence increase with age, then the relationship between age and tardive dyskinesia in a prevalence survey will be even more striking.

The strategy of estimating prevalence in a specific population has limitations, and further advances in our understanding of tardive dyskinesia will require a different type of methodology. Nevertheless, there remain populations of considerable interest for which prevalence estimates would be useful, such as schizophrenic patients who have not received antipsychotic drug treatment, nonpsychotic patients receiving antipsychotic drugs, and individuals with Tourette's disorder. In addition, patients receiving compounds with dopamine antagonist effects (e.g., metoclopramide) for the treatment of gastrointestinal disorders may be at risk for the development of tardive dyskinesia; however, incidence or prevalence in that context has not been established.

Incidence

Incidence refers to the number of new cases occurring in a given population over a specified interval. Some important progress has been made in the last several years involving prospective studies of tardive dyskinesia development. This strategy overcomes many, but not all, of the concerns discussed with regard to cross-sectional prevalence surveys and enables us to develop more accurate estimates of incidence and develop more reliable data bases relevant to the assessment of risk factors.

The limitations of this methodology include the need to maintain the cooperation of large numbers of patients and staff for the duration of a long-term study and the attraction of sufficient funding. In addition, populations with different diagnostic, demographic, and treatment history characteristics should be studied in order to generate results that are applicable and relevant to all types of patients who receive antipsychotic medication.

In follow-up studies, changes in the dose or class of antipsychotic drug in the intervening period between assessments might substantially influence the observed outcome of tardive dyskinesia. For example, an increase in the dose of an antipsychotic drug shortly before reexamination would probably suppress the movements. The condition might then be rated as improved or completely resolved, although the dyskinesia is likely to reappear eventually. In contrast, if antipsychotic drugs were reduced or withdrawn before assessment, this would tend to provoke or increase symptoms (Casey and Gerlach 1986).

Kane et al. (1984, 1986, 1988) reported interim results from a long-term prospective study of tardive dyskinesia. More than 850 patients have entered this study, which involves prospective assessment every 3 months. Patients entering the study are selected without regard to their psychiatric diagnosis or history of antipsychotic drug treatment. A subgroup of approximately 100 of the patients recruited into the study have never received antipsychotic drugs, and this helps to keep the raters blind to medication status.

The average age of the cohort was 29 years, and 43% were female. Of those patients with a history of antipsychotic drug therapy at entry to the study, the median length of lifetime exposure is 12 months, which indicates that patients are followed from a relatively early stage in their drug treatment. The findings thus far are that the cumulative incidence of tardive dyskinesia was 5% at 1 year, 10% at 2 years, 15% at 3 years, and 19% following 4 years of antipsychotic drug exposure. For the fifth and sixth years the figures have continued to increase, being 23% and 26%, respectively.

These results suggest that the cumulative incidence of tardive dyskinesia does increase with increasing duration of antipsychotic drug exposure and that at least for the first several years of such exposure the increase is linear. Whether at some point beyond that the risk decreases remains to be seen, but at the present time it is difficult to identify a period of maximum risk. These data strongly implicate antipsychotic drugs in the development of tardive dyskinesia.

Yassa et al. (1984a, 1984b) carried out a prospective study involving 108 patients (55 men and 53 women) who were assessed over a 2-year period. Almost two-thirds (65%) had a diagnosis of schizophrenia, 12% were suffering from manic depressive illness, 9% had a diagnosis of mental retardation, and 5% had an organic mental syndrome. In 8 patients the tardive dyskinesia persisted through at least two separate examinations at some time during the 2 years. The condition was considered to be of moderate severity in one case and mild in the remainder. An incidence of 7.4% for persistent tardive dyskinesia is given, but this figure is not based on a life-table analysis or a cumulative proportion remaining free of tardive dyskinesia, which would allow inclusion of the dropouts in the incidence calculation. The patients with tardive dyskinesia (mean age 57 years) were significantly older than the nondyskinetic patients (mean age 47 years). The former group had also received antipsychotic drugs for a significantly longer interval (mean 23 years) than the latter group (mean 17 years).

Natural History

The point prevalence figures for tardive dyskinesia at the beginning and end of follow-up studies generally suggest that the proportion of patients