

Use of a VA Pharmacy Database to Screen for Areas at High Risk for Disease: Parkinson's Disease and Exposure to Pesticides

J. A. Yesavage, MD, J. Sheikh, MD, A. Noda, MS, G. Murphy, MD, PhD, R. O'Hara, PhD, R. Hierholzer, MD, M. Battista, PhD, J. W. Ashford, MD, PhD, H. C. Kraemer, PhD, and J. Tinklenberg, MD

ABSTRACT

The purpose of this study was to assess whether pharmacy database information from US Department of Veterans Affairs (VA) medical centers could be used to screen for areas of higher Parkinson's disease prevalence in patients exposed to pesticides. The authors used pharmacy data sets and compared the use of antiparkinsonian medications at 2 VA medical centers in California: one in Palo Alto, near the ocean, and one in Fresno, downwind from extensively farmed parts of the Central Valley. They found that patients at Fresno had higher odds ratios (1.5-1.8) for the use of Parkinson's disease medications than patients at Palo Alto. These data are consistent with the observations of prior epidemiologic studies and suggest that VA pharmacy databases can prioritize locations for further epidemiologic research. However, a thorough exploration of alternative explanations is needed to reach definitive conclusions regarding the findings suggested by this method. (*J Geriatr Psychiatry Neurol* 2003; 16:000-000)

Keywords: pesticides; pharmacy database; Parkinson's disease; epidemiolog

A recent meta-analysis¹ drew the conclusion that at the individual level, the odds ratio for the development of Parkinson's disease (PD) with exposure to pesticides was about 2.0 across a variety of studies. Consistent with this finding is another investigation,² which matched mortal-

ity statistics from California with pesticide use by county and found that the odds ratio for PD with residence in counties with high pesticide use was > 2.0. These were epidemiologic studies seeking to identify risk factors and possible causes of PD. Such studies are difficult to implement in a cost-effective fashion at sites where the prevalence of PD is very low. The purpose of this study was to determine if one can use pharmacy database information from US Department of Veterans Affairs (VA) medical centers to indirectly screen for areas of higher PD prevalence in patients exposed to pesticides, to expedite such epidemiologic studies.

METHODS

We chose to examine the use of antiparkinsonian drugs as an indirect measure of PD. We used local VA clinical pharmacy data sets and compared the use of antiparkinsonian medications at 2 VA medical centers in California. One was in Fresno, which is downwind from extensively farmed parts of the Central Valley. A series of studies designed to examine the effects of pesticide "blow-in" on amphibian populations in the Sierra Nevada Mountains attests that sig-

Received March 12, 2003. Received revised August 18, 2003. Accepted for publication August 21, 2003.

From the Palo Alto Veterans Affairs Health Care System, Palo Alto, California (Drs Yesavage, Sheikh, Ashford, and Tinklenberg); the Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, California (Drs Yesavage, Sheikh, Murphy, O'Hara, Kraemer, and Tinklenberg; Mr Noda); the Central California Veterans Affairs Health Care System, Fresno (Drs Hierholzer and Battista); and the University of California at San Francisco (Drs Hierholzer and Battista).

This research was supported by National Institute on Aging grant AG17824; the Sierra-Pacific Mental Illness Research, Education, and Clinical Center (MIRECC); and the Medical Research Service of the US Department of Veterans Affairs.

Address correspondence to Jerome A. Yesavage, MD, Sierra-Pacific Mental Illness Research, Education, and Clinical Center, Palo Alto VA Health Care System, Palo Alto, CA 94304; e-mail: yesavage@stanford.edu.

DOI: 10.1177/0891988703258672

nificant amounts of pesticide are widely disseminated at a substantial distance from the fields in which they are administered and that Fresno is in the heart of the affected area.³ The other medical center was in Palo Alto, where the prevailing winds are such that few pesticides could blow in from agricultural areas. Thus, we expected a higher prevalence of PD at the Fresno VA facility than at the Palo Alto facility.

RESULTS

For each of the years from 1997 to 2001, we counted the numbers of patients who were prescribed the common antiparkinsonian drug carbidopa/levodopa at both the Palo Alto and Fresno VA centers. In addition, we counted the total number of patients at each VA center who received drug prescriptions of any kind. Note that a patient may be given prescriptions over the course of several years. The prevalence of carbidopa/levodopa among all prescriptions was then calculated for each year as an indicator of prevalence rates at the Fresno and Palo Alto VA centers (see Table 1).

DISCUSSION

The odds ratios of 1.5 to 1.8 for PD at Fresno, which we calculated using VA pharmacy data, are consistent with the observations of other individual studies, cited above, which found higher odds ratios for PD with higher pesticide exposure. This suggests that VA pharmacy databases may be used to screen for areas particularly relevant for study in large-scale epidemiologic work. Recently, the VA has created a consolidated national database that will contain similar data to those used in this study. This technique may be of use in other situations in which a medication is consistently used for one indication and rarely used for any others. In the future, information from the national pharmacy database, which is collected by the Pharmacy Benefits Management Strategic Health Group of Hines, Illinois, may also be merged with clinical data from the VA's main database in Austin, Texas. Such merges, though technically possible, are difficult and time consuming because of the many administrative and security approvals necessary. They are also subject to problems associated with the potential for incompleteness, inaccuracies, and incomparability in data abstracted from essentially clinical sources. Nonetheless, it is expected that more analyses will be performed with merged clinical and pharmacy data because that will allow substantially richer analyses, including, for example, diagnostic and extensive psychosocial information.

Despite the potential usefulness of this approach to screen for areas that might be at high risk for the development of PD, we emphasize the preliminary nature of our report, and there are a number of important methodological considerations and limitations that must be empha-

Table 1. Differential Antiparkinsonian Medication Prescriptions per Patient at the Fresno and Palo Alto, California, Veterans Affairs Facilities

	1997	1998	1999	2000	2001
Fresno					
Carbidopa/levodopa prescriptions	111	154	176	182	210
Total prescriptions	10,256	13,594	14,491	14,599	16,487
Antiparkinson prescriptions/all prescriptions	0.0108	0.0113	0.0121	0.0125	0.0127
Palo Alto					
Carbidopa/levodopa prescriptions	176	188	211	225	290
Total prescriptions	23,795	27,386	30,048	31,961	34,557
Antiparkinson prescriptions/all prescriptions	0.0074	0.0069	0.0070	0.0070	0.0084
Odds ratio (Fresno/Palo Alto)	1.5	1.6	1.7	1.8	1.5
Lower 95% confidence interval	1.1	1.3	1.4	1.5	1.3
Upper 95% confidence interval	1.9	2.1	2.1	2.2	1.8

sized. We assumed in our analyses that disease misdiagnosis rates and drug utilization rates are similar between VA hospitals. This fact, however, is not established, and one might be able to argue, for example, for the existence of hospital-to-hospital differences between urban and rural areas, between teaching hospitals and others, between hospitals serving older populations and those serving younger populations, and between hospitals with greater smoking rates and those with lower rates. The identification of hospitals with greater prevalences of PD might be enhanced by the consideration of such sources of “ecological” differences. In fact, the database itself might be used to determine if prescribing practices differ across sites.

However, the “ecological fallacy” refers to attempting to draw inferences at the individual level from analyses done at the ecological (here, hospital) level. Thus, finding sources of interhospital differences could not be interpreted as finding risk factors for PD, and certainly, one cannot draw causal inferences from observational studies. Thus, although the VA medication database can become a useful screening tool to identify sources of patients for epidemiologic studies, any attempt at conducting a valid epidemiologic study would require the sampling of individual patients within each source, careful diagnosis, and the collection of many other types of information.

We also note that if all PD patients were treated with carbidopa/levodopa, and non-PD patients were never prescribed the drug, its prevalence would be exactly equal to that of PD. On the other hand, some patients with PD may not be properly diagnosed or may not be treated with the drug, and some non-PD patients may be treated with the drug. In that case, the prevalence of the drug would be highly correlated with, but not equal to, the prevalence of PD. The odds ratio of the prevalence of the drug's use

would be an attenuated estimate of the prevalence of PD at each site. Under the assumption that the false positive and false negative rates are similar across VA sites, the odds ratio of the prevalence of the drug's use would be an attenuated estimate of the odds ratio of the prevalence of PD. Across multiple sites, the odds of the prevalence of the drug's use would order the sites in the same order as would the odds of the prevalence of PD.

The questions also arise of what one might do with this information and why one needs to be concerned with screening for areas of high PD prevalence. We expect that some of the excess PD found in the vicinity of Fresno County may be due to both agricultural workers' pesticide exposures and drift blow-in to nonagricultural workers who may be susceptible to the disease. One possible application is to study ecological correlations in more detail. For example, if one wished to test whether exposure to pesticides correlates with PD prevalence at the ecological level, one could sample communities and correlate community exposure and drug prevalence. The database could also be used to study incidence and prevalence rates longitudinally under continuing exposure to an alleged toxin. Furthermore, there is growing literature suggesting that genetic variation may explain why some individuals develop PD after exposure to environmental toxins, whereas others do not.³⁻⁵ Pharmacy database information could be used to help

identify geographical areas where genetic variants associated with high vulnerability to neurotoxic exposure are most likely to become clinically (ie, phenotypically) apparent in large, expensive genetic epidemiologic studies.

Thus, it may be that the systematic use of pharmacy database information to identify locations at high risk for the development of PD might form the basis of selecting hospitals with high enough base rates to support detailed and cost-effective epidemiologic studies, randomized clinical trials of new treatments, or efforts to limit the further exposure of patients to pesticides through patient education efforts.

References

1. Priyadarshi A, Khuder SA, Schaub EA, Shrivastava S. A meta-analysis of Parkinson's disease and exposure to pesticides. *Neurotoxicology* 2000; 21(4):435-440.
2. Ritz B, Yu F. Parkinson's disease mortality and pesticide exposure in California 1984-1994. *Int J Epidemiol* 2000; 29(2):323-329.
3. Giasson BI, Lee VM. A new link between pesticides and Parkinson's disease. *Nat Neurosci* 2000; 3(12):1227-1228.
4. Checkoway H, Nelson LM. Epidemiologic approaches to the study of Parkinson's disease etiology. *Epidemiology* 1999; 10(3):327-336.
5. Veldman BA, Wijn AM, Knoers N, et al. Genetic and environmental risk factors in Parkinson's disease. *Clin Neurol Neurosurg* 1998; 100(1):15-26.