Clinical Nonrecognition of Neuroleptic-Induced Movement Disorders: A Cautionary Study

Peter J. Weiden, M.D., J. John Mann, M.D., Gretchen Haas, Ph.D., Marlin Mattson, M.D., and Allen Frances, M.D.

Extrapyramidal side effects are a major limitation in the use of neuroleptics, and tardive dyskinesia is a special public health problem. Accurate clinical diagnosis of extrapyramidal syndromes is necessary for effective management. The authors compared clinicians' recognition of the major extrapyramidal syndromes in 48 psychotic inpatients with independent blind diagnoses by clinical researchers using standardized ratings. The major finding was a high rate of clinical underrecognition of all major extrapyramidal syndromes, especially tardive dyskinesia. The authors discuss the clinical predictors of nonrecognition of extrapyramidal side effects and recommend improved training in their detection.


Extrapyramidal side effects of neuroleptics (dystonia, akathisia, akinesia, parkinsonism, and tardive dyskinesia) must be promptly recognized to maximize compliance (1), decrease iatrogenic complications, and improve the patient's quality of life (2, 3). Effective management of extrapyramidal side effects depends on the ability of clinicians who prescribe neuroleptics to make accurate diagnoses.

Previous anecdotal reports have noted misdiagnosis of dystonia (4) and akathisia (5) and difficulty in distinguishing akinesia from depression (6). There is also evidence that tardive dyskinesia is underreported by patients (7) and that its severity can be underestimated by clinicians (8). Chronic parkinsonian and dyskinetic syndromes secondary to neuroleptic treatment have been misdiagnosed in medical and neurologic clinics (9, 10). Chronic psychiatric patients evaluated in psychiatric clinics have been shown to have a high prevalence of mild tardive dyskinesia but only when diagnosed by expert raters (11).

Although this anecdotal evidence suggests major clinical problems in the accurate diagnosis of neuroleptic-induced extrapyramidal side effects, to our knowledge only one study (12) has systematically evaluated discrepancies between research and clinician diagnoses of tardive dyskinesia. The purpose of our study was to assess prospectively the level of detection of extrapyramidal syndromes achieved by the attending psychiatrists and psychiatric residents routinely managing psychotic patients in the acute inpatient psychiatric units of a university medical center. The results help to explain discrepancies in the rates of extrapyramidal side effects between clinical and re-
search studies and have serious implications for clinical practice and training.

**METHOD**

We studied 58 patients who had been consecutively admitted to the three acute inpatient units of Payne Whitney Psychiatric Clinic and who met the study criterion of having an acute psychosis without a known organic mental syndrome. Within 48 hours of admission and then weekly until discharge, each patient was rated by at least one researcher (P.J.W. or J.J.M.) who was blind to the clinician’s diagnosis or treatment of extrapyramidal syndromes. All clinical staff were kept blind to the purpose of the study.

**Ratings of Extrapyramidal Symptoms**

The presence and severity of parkinsonism, akinesia, akathisia, dystonia, and tardive dyskinesia were determined by the researchers with modifications of the Webster Parkinson’s disease scale (13), the akinesia scale of Rifkin et al. (14), the Van Putten akathisia scale (15), the Extrapyramidal Symptom Rating Scale (16), and the Abnormal Involuntary Movement Scale (AIMS) (17).

The research diagnosis of tardive dyskinesia was based on an AIMS global score of 2 or higher and was confirmed by independent assessment by a second rater. For parkinsonism, akinesia, and akathisia, the research diagnosis was based on a rating of 2 or higher on a 4-point global scale, which corresponds clinically to a range of mild (but unequivocal) to severe symptoms. Dystonia was assessed by means of the Extrapyramidal Symptom Rating Scale, which determines either its presence or absence, and patient reports of a history of dystonia.

The clinicians’ diagnoses of extrapyramidal side effects were established through chart review (by P.J.W.) after each patient’s discharge. The results of the physical examination at admission, emergent physical findings, the patient’s complaints, nurses’ observations, recorded quotations and handwriting samples from the patient, family comments, and the physician’s differential diagnosis of changes in the patient’s behavior consistent with neuroleptic-induced extrapyramidal side effects were reviewed systematically. Medication histories (neuroleptic doses and dose changes, anticholinergic or other treatments, and “p.r.n.” treatments for extrapyramidal side effects) were recorded. Clinical observations of extrapyramidal symptoms derived from the chart over the hospital course were contrasted with the patient’s research ratings.

The following operational criteria for clinician nonrecognition of extrapyramidal side effects were chosen to standardize the assessment of clinical diagnostic accuracy: 1) nonrecognition by the physician of moderate dystonia of mild or greater severity, 2) failure to recognize acute dystonia when its symptoms were observed by staff or reported by the patient, 3) failure to document moderate rigidity or tremor within 1 week of detection by research assessment, 4) physician’s failure to consider akinesia or akathisia as a diagnostic possibility within 1 week of onset of typical behavioral or motoric symptoms.

**Characteristics of Unit Staff and Patients**

The staff on each of the 24-bed units included two full-time supervising attending psychiatrists, four psychiatry residents in postgraduate year 2, and one inpatient chief resident in postgraduate year 4. The data were collected between August and October, the second through fourth months of the residents’ second-year inpatient experience. The residents had also completed 5 months of psychiatric training during their internships and a course on the inpatient treatment of acute psychosis. All trainees had at least two attending supervisors who periodically examined all of their patients.

Of the 58 patients examined, 48 received at least 1 week of continuous neuroleptic treatment and completed at least two research ratings of extrapyramidal side effects. These 48 patients were relatively young (mean±SD age=27.4±16.9 years) and consisted of 29 females and 19 males. Their DSM-III diagnoses at discharge included schizophrenia (N=19), schizoaffective disorder (N=12), schizophraniform disorder (N=3), bipolar disorder, manic or mixed (N=9), and major depression with psychotic features (N=5). Their mean±SD length of stay was 28.0±14.6 days, and they received 3.6±1.7 research ratings. The average dose of neuroleptics during acute treatment was 1401±1064 mg/day of chlorpromazine equivalents, and the range was 200–5000 mg/day. Initial anticholinergic prophylaxis was begun for 29 patients (60%), and eventually 44 patients (92%) received adjuvant anticholinergic therapy. Of note in the clinical management of this group are the relatively high neuroleptic doses used and the high frequency of administration of anticholinergic agents.

The number of patients in whom extrapyramidal side effects were identified by means of the standard research assessments was high. Of the 48 patients, 29 developed parkinsonian signs, 23 had akinesia (all of these patients had coexisting parkinsonian signs), 27 had akathisia, three had dystonic reactions during research examinations, and 11 had dystonias according to the combination of clinical diagnosis and research dystonia history. Ten patients (out of the original 58) had tardive dyskinesia.

**RESULTS**

Each patient who had extrapyramidal side effects according to the researcher’s diagnosis was categorized in terms of presence or absence of an accurate clinical diagnosis. Table 1 reveals striking and highly signifi-
TABLE 1. Research and Clinical Diagnoses of Neuroleptic-Induced Extrapyramidal Syndromes in 48 Psychotic Patients

<table>
<thead>
<tr>
<th>Extrapyramidal Syndrome</th>
<th>Patients Given Research Diagnosis</th>
<th>Patents Given Clinical Diagnosis</th>
<th>Percent of Patients Given Research Diagnosis</th>
<th>McNemar Test of Difference Between Clinician and Researcher Errors</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>$\chi^2$ (df=1) $p$</td>
</tr>
<tr>
<td>Dystonia</td>
<td>3</td>
<td>1</td>
<td>33</td>
<td>-</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>29</td>
<td>17</td>
<td>59</td>
<td>10.08 $&lt;.005$</td>
</tr>
<tr>
<td>Akinesia</td>
<td>23</td>
<td>14</td>
<td>61</td>
<td>7.11 $&lt;.01$</td>
</tr>
<tr>
<td>Akathisia</td>
<td>27</td>
<td>7</td>
<td>26</td>
<td>18.05 $&lt;.001$</td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
<td>10</td>
<td>1</td>
<td>10</td>
<td>7.11 $&lt;.01$</td>
</tr>
</tbody>
</table>

*Total sample included 58 patients.

TABLE 2. Global Severity of Extrapyramidal Syndromes in Cases Recognized and Unrecognized by Clinicians

<table>
<thead>
<tr>
<th>Extrapyramidal Syndrome</th>
<th>Recognized by Clinician</th>
<th>Unrecognized by Clinician$^1$</th>
<th>Comparison of Ratings</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Patients</td>
<td>Severity Rating</td>
<td>Patients</td>
</tr>
<tr>
<td></td>
<td>Mean SD</td>
<td></td>
<td>Mean SD</td>
</tr>
<tr>
<td>Parkinsonism</td>
<td>17</td>
<td>2.38 (0.59)</td>
<td>12</td>
</tr>
<tr>
<td>Akinesia</td>
<td>14</td>
<td>2.70 (0.80)</td>
<td>9</td>
</tr>
<tr>
<td>Akathisia</td>
<td>7</td>
<td>3.14 (0.64)</td>
<td>20</td>
</tr>
<tr>
<td>Tardive dyskinesia</td>
<td>Global</td>
<td>2.50 (0.58)</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Oral</td>
<td>2.75 (0.50)</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Extremitiy</td>
<td>1.50 (1.29)</td>
<td>6</td>
</tr>
<tr>
<td></td>
<td>Extremitiy/total$^2$</td>
<td>0.24 (0.36)</td>
<td>6</td>
</tr>
</tbody>
</table>

$^1$See text for definition of undiagnosed cases.

$^2$Sum of the AIMS extremity movement items divided by the sum of the AIMS facial and oral movement items.

cient rates of disagreement between the research and clinical diagnoses across all types of extrapyramidal side effects. Except for three cases of dystonia, all the cases of extrapyramidal side effects documented by the clinical method were picked up by the research method, but many cases were missed by the clinicians but detected by the research assessment. There was no significant difference between the patients whose extrapyramidal side effects were and were not recognized clinically in terms of demographic characteristics, discharge diagnoses, rates of anticholinergic prophylaxis, or (except for akathisia) neuroleptic doses.

Only one of the 10 patients with tardive dyskinesia was accurately diagnosed by the clinicians. Among the nine patients with undiagnosed cases, three had nurse or physician notes that mentioned abnormal dystonic movements but no follow-up diagnosis of tardive dyskinesia. Considering these three cases as recognized cases of tardive dyskinesia allows a comparison of four "recognized" and six unrecognized cases. Overall severity on the global AIMS did not discriminate the patients with recognized and unrecognized cases (see table 2). However, oral movements were significantly more severe in the patients with recognized tardive dyskinesia, whereas the patients with unrecognized cases had a predominance of extremity movements.

Mild parkinsonism (tremor, rigidity, micrographia, or decreased fine motor coordination) was found by the researchers in 29 patients. Rigidity was the most severe clinical sign in 26 of them. In 17 cases the parkinsonism was accurately diagnosed by the clinician. Of the 12 cases that were inaccurately diagnosed, eight were missed completely, two were identified with a delay of more than 1 week, and two were underrated in global severity. The mean researcher ratings of global severity for the unrecognized and recognized cases of parkinsonism did not significantly differ (table 2), suggesting that overall clinical severity did not determine nonrecognition.

Of the 23 researcher-diagnosed cases of akinesia, 14 were accurately identified by clinicians. Among the nine missed cases, five had no diagnosis or no mention of the differential diagnosis of akinesia, three received the likely misdiagnosis of "depression" (without consideration of the possibility of akinesia despite the temporal correlation of akinesia with neuroleptic administration), and one was severe but was rated by clinical staff as "mild" and received no treatment. Severity of symptoms predicted clinical diagnostic accuracy but in an unexpected direction. The cases missed by the clinicians had significantly more severe symptoms than the recognized cases (table 2). Patients with misdiagnosed akinesia were also significantly more likely to suffer from coexisting akathisia ($t=3.8$, df=21, p<.001).

The clinical staff inaccurately diagnosed 20 of the 27 researcher-diagnosed cases of akathisia. The clinical errors consisted of nine cases in which the akathisia went unnoticed, seven cases of errors in the differential diagnosis of agitation/restlessness/"acting out" after
recent increases in neuroleptic dose, and four cases of delay in diagnosis of more than 1 week. Underrecognition of akathisia was significantly associated with lower severity research ratings, suggesting that milder (or less reliably ratable) forms of akathisia are missed in clinicians’ assessments. In addition, the patients with unrecognized akathisia received higher neuroleptic doses than the patients with diagnosed akathisia (mean±SD=1700±935 versus 1007±406 mg/day of chlorpromazine equivalents; t=2.6, df=25, p<.01). The patients with undiagnosed akathisia also suffered from more severe coexisting akinesia than those with accurate akathisia diagnoses (t=2.8, df=25, p<.05).

Acute dystonic reactions were difficult to assess accurately on the basis of patient reports because of the patients’ poor recall and unreliable descriptions of dystonias. Chart review revealed three cases of dystonias missed by systematic research assessment with the Extrapyramidal Symptom Rating Scale. In contrast, however, three patients had acute dystonias during research examinations (two had oculogyric crises and one had neck torticollis); all occurred early in the course of neuroleptic treatment. In all three cases, the patients complained of their symptoms to the nursing staff. Two were misdiagnosed: one was described as “psychotic behavior” by the physician on call, and the other was considered “hysteric” by the nursing staff and received no physician evaluation. No treatment was given to either patient.

Each patient (N=16) who gave a preadmission history of distressing acute extrapyramidal side effects during previous neuroleptic exposure received anticholinergic prophylaxis. However, presence or absence of anticholinergic prophylaxis was not a predictor of subsequent physician nonrecognition of extrapyramidal syndromes. Every case of acute extrapyramidal side effects that was clinically diagnosed was initially treated with adjuvant medication, never with a reduction of neuroleptic dose.

**DISCUSSION**

The major finding of this study was a high rate of clinician nonrecognition of extrapyramidal side effects. This finding suggests that wide differences in the frequency of extrapyramidal side effects across studies may be partly due to variations in the expertise and sensitivity of the examiners. These results definitely point to severe limitations in using chart review alone in quality assurance studies to determine the nature and extent of extrapyramidal side effects. Most important clinically, however, are the serious yet correctable blind spots in the clinical diagnosis of extrapyramidal side effects. We wish to emphasize that there was nothing difficult about the research evaluation of extrapyramidal symptoms and that clinical nonrecognition of extrapyramidal side effects can be reduced with better training and systematic attention to this problem.

Tardive dyskinesia, despite its persistent nature, is often missed, especially when its symptoms involve the extremities rather than the “classic” orobuccal areas. This selective nonrecognition of extremity dyskinesias may arise for several reasons: this form of tardive dyskinesia is less well known to clinicians, patients may disguise their hand dyskinesias better than oral ones, hand dyskinesias often occur only when the patient is walking, shoes usually are not removed during examinations, and hand choreas may be mistaken for tremors. Physicians should inspect the extremities for choreiform movements and generally have a high index of suspicion for any form of tardive dyskinesia in any patient receiving antipsychotic medications.

Severe forms of akinesia tend to be more frequently underrecognized than milder cases. This may be because severely akinetic patients complain less about their symptoms than patients with milder cases or because severe akinesia is more likely to be misdiagnosed as depression. Akinesia should be considered in the differential diagnosis of any patient taking neuroleptics who becomes amotivational, depressed, lethargic, or slowed down. Staff cannot expect the patient to report these changes spontaneously.

- The higher neuroleptic doses found in the patients with unrecognized akathisia than in those with recognized akathisia may reflect the eventual appropriate lowering of neuroleptic dose when the akathisia was diagnosed. For those patients whose akathisia is misdiagnosed as agitation or psychosis, the neuroleptic dose will instead be increased. Akathisia also seemed to be missed when it presented behaviorally (i.e., as an elopement or incident requiring seclusion) or when the patient was too psychotic, disorganized, or akinetic to complain of akathisia. In the very psychotic patient, the subjective experience of akathisia can only be assessed (if at all) by a direct, focused patient interview. In fact, akathisia should be considered for any restlessness, agitation, or acting-out behavior of recent onset that temporarily coincides with escalating neuroleptic dose, even if the patient does not voluntarily mention severe inner restlessness. The clinician should not rule out akathisia until completing such a focused, active inquiry for subjective restlessness and/or behavioral agitation.

Dystonia was the only extrapyramidal side effect missed by research rating but not clinical diagnosis, suggesting that dystonias cannot be accurately ascertained by interview alone. The intermittent nature of dystonias usually requires that an assessment be made by means of patient history rather than physical examination. Unfortunately, the historical method for diagnosing dystonias proved to be unreliable. Even more discouraging was what happened with the acute dystonias actually observed by both researchers and staff. Despite the small number of such cases, an unequivocal rate of 67% for the misdiagnosis of typical and classic dystonias is noteworthy, and it seems that textbook cases of acute dystonia are still
frequently attributed to psychopathology. The dystonias in our study seemed to be missed because they occurred shortly after admission, when the staff did not know the patients, some of whom were very psychotic. Other immediate management issues seemed to preempt the careful observation necessary to make a diagnosis of dystonia. We therefore recommend that all inpatient staff automatically consider any new muscle spasm or posturing arising early in neuroleptic treatment to be a dystonic reaction.

Other useful diagnostic techniques include a focused clinical interview with repeated attempts to elicit complaints of all subtypes of extrapyramidal side effects, interviewing family members about the patient's current behavior and whether it coincides with extrapyramidal side effects in the past, and being cautious about any report or past history of "hysterical" or "psychotic" abnormal movements. Another helpful technique is a review of the timing and doses of all medications administered to find pharmacologic correlates with the undiagnosed behavior. Graphing the medication record alongside recorded observations of the patient's symptoms can highlight medication-induced toxicity patterns.

The clinicians in this study consistently provided anticholinergic prophylaxis for patients who gave prior histories of extrapyramidal side effects. They also promptly treated diagnosed extrapyramidal symptoms with adjuvant medication. However, it is striking that neuroleptic dose reduction was never the initial treatment when such a symptom was recognized. It seems that lowering the neuroleptic dose should have been used more often. In addition, using prophylactic anticholinergic agents did not improve the recognition rate. Therefore, clinicians should not be lulled into a false sense of security by the belief that anticholinergic prophylaxis solves the problems of accurately assessing extrapyramidal side effects.

This study of clinician versus research diagnosis of extrapyramidal symptoms has several limitations. The clinician diagnoses were determined by means of retrospective chart review, which depends on accurate chart documentation and may have underestimated the rates of actual clinician diagnoses of extrapyramidal side effects. This retrospective method was chosen to avoid alerting the clinicians to the nature of the study. However, since the necessity for documenting extrapyramidal side effects is carefully emphasized at our institution and the charts are well documented in other ways, it seems unlikely that a diagnosis of an extrapyramidal syndrome would not have become part of the treatment record.

Another potential methodologic problem of this study is the lack of research rater blindness to the purpose of the study. This may have inflated the number of research diagnoses of extrapyramidal side effects, resulting in an artificially high rate of clinical nonrecognition. However, the rates of clinical nonrecognition across all subtypes of extrapyramidal symptoms (except akathisia) did not proportionately decrease as the researcher-rated severity increased. It was not just subtle extrapyramidal effects that were not recognized, but unequivocal ones as well. Weekly movement disorder research rounds served as reliability checks of the primary raters (P.J.W. and J.J.M.). Therefore, we feel researcher bias does not explain these results.

Another concern is that there is a high degree of intrinsic overlap in the presentations of certain extrapyramidal side effects and primary psychiatric diagnoses and that the research rater may have mistaken primary psychopathology for extrapyramidal side effects. This is most possible for the research-diagnosed akinesia and akathisia. Although we cannot rule out the possibility that symptom overlap increased the researcher diagnoses of extrapyramidal side effects, the same difficulties face the treating clinical teams, who need to routinely consider akathisia and akinesia in the differential diagnoses of sudden, unexplained behavioral changes (4-6). Indeed, the researchers performing the chart reviews accepted as an accurate clinical diagnosis any documentation that included extrapyramidal side effects as part of the differential diagnosis regardless of the final conclusion. Moreover, seemingly "hard" and unequivocal neurologic findings such as dystonia and dyskinesia were missed at even higher rates than akinesia and akathisia.

Other methodologic questions relate to the relevance and generalizability of these findings to nationwide patterns in the diagnosis of extrapyramidal side effects. It is possible that these results reflect a particular blind spot of the institution where the study was performed. A related issue is the timing of the study, which occurred early in the 12-month training cycle; the results may differ with more experienced residents. We think that this is an inadequate explanation of our findings given that the residents were well qualified and were supervised by full-time attending physicians. Furthermore, a similar chart review conducted at a Veterans Administration teaching hospital (12) also demonstrated a 75% rate of nonrecognition of tardive dyskinesia by clinical staff, strongly suggesting the possibility of a nationwide pattern of nonrecognition of extrapyramidal side effects. We suspect that the underdiagnosis of extrapyramidal side effects reflects the clinical limitations of attending and resident psychiatrists who are not specifically and extensively trained in the evaluation of extrapyramidal symptoms and who do not systematically rate them at regular intervals.

The ability to perform a sophisticated assessment of extrapyramidal side effects is not easily learned and requires specific training. This study underscores the need for careful supervision, training, and attention to the accurate diagnosis of extrapyramidal side effects. It also seems clear that repeated and systematic evaluation of extrapyramidal symptoms with standardized measures (at least every 2 weeks and at admission and discharge) should be made routine on every acute inpatient unit. General psychiatric interviewing meth-
ods and mental status examinations without specific and systematic examinations for extrapyramidal side effects may distract clinicians by providing spurious psychologic explanations for neuroleptic-induced motoric and behavioral changes. Without significant remediation of errors in diagnostic methods and training insufficiencies, it is likely that extrapyramidal side effects will continue to be underdiagnosed at an alarmingly high rate.

REFERENCES

15. Van Putten T: Why do schizophrenic patients refuse to take their drugs? Arch Gen Psychiatry 1974; 31:61-72

Deceased Members of the American Psychiatric Association

The deaths of these members were reported to APA between April 15, 1987, and June 10, 1987.

Jose Rolando Ariasaga
Willard D. Boaz
Charles Buckman
Carmelo Camillo
Gerald C. Crary
G. Cameron Cray
Elisabeth B. Goldner
Nandkishor K. Gujrathi
Philip R. Hastings
Lynda Janice Howieart
Victor H. Hunkel
Robin C. Hunter
Albert John Kazlauskas
Rudolph Kieve
John Tarlton Morrow, Jr.
Mollie E. Orloff
Malcolm Paine
Veronica M. Pennington
Michael R. Peterson
Tristan E. Shipley
Louis Stix
Anthony S. Tornay
Paul D. Williams