Accuracy of diagnosis in patients with presumed Parkinson’s disease

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Abstract

Objectives: to study the diagnostic accuracy for parkinsonism and Parkinson’s disease in a community-based sample of subjects on anti-parkinsonian medication.

Methods: computerized prescribing records in general practice were used to create a community-based disease register for Parkinson’s disease. Subjects were examined to establish the likely diagnosis using recommended clinical diagnostic criteria.

Results: of 402 cases, parkinsonism was confirmed in 74% and clinically probable Parkinson’s disease in 53%. The commonest causes of misdiagnosis were essential tremor, Alzheimer’s disease and vascular pseudo-parkinsonism. Over one-quarter of subjects did not benefit from anti-parkinsonian medication.

Conclusions: there is difficulty in diagnosing parkinsonism and Parkinson’s disease in elderly subjects and we suggest early referral of those suspected of having parkinsonism for specialist assessment.

Keywords: diagnosis, drug treatment, parkinsonism

Introduction

Parkinsonism is relatively common in elderly subjects [1], although diagnosis may be difficult in this group. In cross-sectional studies, at least two-thirds of patients with the diagnosis of Parkinson’s disease are over the age of 70 years. The incidence of subtle extrapyramidal signs on neurological examination of elderly subjects with no known neurological or psychiatric disease is high, with recorded prevalences in subjects over 65 years old of 32% [2] and 35% [5]. Prevalence estimates for clinically-evident parkinsonism in similarly aged subjects are much lower (around 3%). Prevalence studies of parkinsonism based on ascertainment by a combination of methods suggest a diagnostic accuracy of 80% after examination and the application of clinical diagnostic criteria [4–7]. The commonest causes of misdiagnosis of parkinsonism are essential tremor, vascular pseudo-parkinsonism and Alzheimer’s disease [8].

There are further difficulties in distinguishing Parkinson’s disease from other causes of parkinsonism. Recent clinico-pathological studies have demonstrated a diagnostic accuracy for Parkinson’s disease of only 76% [9–11]. Multi-system atrophies and Alzheimer’s disease accounted for most misdiagnosed cases [10].

Few subjects with parkinsonism and other involuntary movement disorders are diagnosed and managed long-term in health care without specialist assessment and diagnosis. We have examined diagnostic accuracy for both parkinsonism and Parkinson’s disease in a cross-sectional community sample of individuals with presumed Parkinson’s disease and receiving anti-parkinsonian drug treatment.

Methods

Cases of presumed Parkinson’s disease of all ages were identified from 74 general practices in North Wales. All but one practice agreed to participate. Ascertainment of cases was made by the identification of individuals in receipt of anti-parkinsonian drugs. Nearly all practices used computerized prescribing which could readily generate a list of subjects on anti-parkinsonian medication. Cases of drug-induced parkinsonism as a result of neuroleptic treatment of mental illness were excluded. Patients were visited at home or seen in a specialist movement disorder clinic, where a history was taken and a neurological examination performed.

Diagnosis was based on the history, examination, medical records and the application of recommended clinical diagnostic criteria for Parkinson’s disease [12], multiple system atrophy [13], progressive supranuclear palsy [14] and other non-parkinsonian diagnoses such as essential tremor [15] and Alzheimer’s disease [16].
The diagnostic criteria used for Parkinson’s disease are shown in the Appendix. These criteria have been shown, when applied retrospectively, to improve the diagnostic accuracy of cases of presumed Parkinson’s disease referred to a brain bank [10]. In this situation the criteria had a sensitivity of 96% and a specificity of 82% for the diagnosis of Parkinson’s disease compared to established neuropathological criteria. Results

Out of 502 cases of presumed Parkinson’s disease from the participating practices, 402 were examined. A total of 44 subjects declined to take part. The remaining 56 subjects were not visited at home due to travelling distance and resource constraints. The median number of subjects per practice was 5.7 (range 1–36), this large range reflecting practice size and location. The mean age of subjects was 76 (range of 33–94 years). Mean age of onset of symptoms was 67 years. Mean duration of disease was 8 years. More than 80% of subjects were over 60 at the time of the study.

A definite diagnosis of Parkinson’s disease was made in 213 (53%) cases (Table 1). Parkinsonism that either did not meet the full clinical diagnostic criteria or was clearly due to some other cause accounted for a further 86 (21%) cases. Drug-induced parkinsonism accounted for 12 (3%) of these cases. In total, parkinsonism was confirmed in 299 (74%) subjects. The cause of parkinsonism was judged to be clinically probable Parkinson’s disease in 213 (71%) of these 299 cases.

Essential tremor was diagnosed in 50 of the remaining 103 (29%) subjects in whom parkinsonism could not be demonstrated (Table 2). Gait apraxia due to vascular pseudo-parkinsonism and individuals with dementia pre-dating the onset of mild extrapyramidal signs accounted for the remaining cases that were not true parkinsonism.

The diagnosis of Parkinson’s disease/parkinsonism and the initiation of treatment was made by the general practitioner in 59% of cases.

Discussion

Both parkinsonism and Parkinson’s disease are difficult to diagnose since over one-quarter of cases had no clinical evidence of parkinsonism when examined.

The diagnosis of probable parkinsonism and Parkinson’s disease, despite advances in neuroimaging, is still determined by accurate history and examination. Diagnostic accuracy in epidemiological studies depends upon the careful and correct use of clinical diagnostic criteria. Past epidemiological studies have used combinations of historical features and physical signs for the diagnosis of parkinsonism and Parkinson’s disease. These have often been applied retrospectively from medical records or the diagnosis has been based on medical records or drug prescription alone. The accuracy of past diagnostic criteria have not been compared with the standard of neuropathological diagnosis. In this study, the diagnosis of parkinsonism and Parkinson’s disease was based on the application of clinical diagnostic criteria for Parkinson’s disease validated by neuropathological studies and developed by the Parkinson’s Disease Society Brain Bank. Other recent epidemiological studies of Parkinson’s disease have adopted these criteria [7, 17].

A good or excellent response to levodopa therapy is strongly suggestive of a diagnosis of Parkinson’s disease. In patients presenting for diagnosis tests of dopaminergic responsivity, a single dose of levodopa or apomorphine can be helpful in confirming Parkinson’s disease. However, a negative test does not rule out a positive response to longer-term oral treatment and patients with parkinsonism not due to Parkinson’s disease can respond initially to dopaminergic drugs [18].

Clinically probable Parkinson’s disease was found in just over half the subjects in the study although, even using clinical diagnostic criteria, up to 20% of this group will not have typical Parkinson’s disease pathology at post mortem [10].

Essential tremor, Alzheimer’s disease, and vascular pseudo-parkinsonism caused most of the diagnostic difficulty in determining the presence or absence of parkinsonism. In one of the earliest community-based

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Table 1. Diagnosis of subjects (n = 402) with presumed Parkinson’s disease

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (and %) of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parkinsonism</td>
<td>299 (74%)</td>
</tr>
<tr>
<td>Probable Parkinson’s disease</td>
<td>213 (53%)</td>
</tr>
<tr>
<td>Possible Parkinson’s disease and parkinsonism clearly due to other causes</td>
<td>86 (21%)</td>
</tr>
<tr>
<td>Parkinsonism not detected</td>
<td>103 (26%)</td>
</tr>
</tbody>
</table>

Table 2. Revised diagnosis of subjects (n = 103) without parkinsonism

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>No. (and %) of subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essential tremor</td>
<td>50 (48%)</td>
</tr>
<tr>
<td>Gait apraxia</td>
<td>57 (56%)</td>
</tr>
<tr>
<td>Dementia preceding motor signs</td>
<td>16 (16%)</td>
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</tbody>
</table>
studies of Parkinson’s disease, essential tremor accounted for 26% of cases of presumed Parkinson’s disease [4]. Resting tremor can occur in essential tremor [19], which further complicates diagnosis. Alzheimer’s disease is more commonly associated with extrapyramidal signs than previously thought and, unless a history of dementia is carefully sought which pre-dates the onset of extrapyramidal signs, this can be a further cause of misdiagnosis [10]. A further source of diagnostic difficulty in elderly subjects is vascular pseudo-parkinsonism. Attenuation of the periventricular white matter and basal ganglia is associated with gait apraxia with axial rigidity but preservation of facial movements and no evidence of upper limb akinesia.

In this study, 71% of cases of parkinsonism were thought to be clinically probable Parkinson’s disease. This figure is consistent with most epidemiological studies of parkinsonism, where drug-induced parkinsonism and multi-system disorders account for the remainder [20–22]. A total of 3% of cases had drug-induced parkinsonism unrelated to the neuroleptic treatment of mental illness.

At least one-quarter of subjects in this study would not have derived any benefit from anti-parkinsonian medication and only about a half of the subjects were likely to derive benefit from therapy. Drugs used in the treatment of Parkinson’s disease are often associated with side effects in elderly subjects. In particular, dopaminergic drugs can impair cognitive function and cause postural hypotension. The likely benefit of drug treatment in the remaining subjects is difficult to assess, since many patients not fulfilling diagnostic criteria for Parkinson’s disease will have this disease and be responsive to treatment and of cases of multiple system atrophy and progressive supranuclear palsy may respond transiently to levodopa treatment.

This study also demonstrates the problems in using drug prescription as a surrogate for diagnosing Parkinson’s disease in epidemiological prevalence studies. Drug prescription will fail to detect medically unknown but clinically symptomatic cases [21, 23–25] and will also fail to detect medically known cases not on treatment [21, 23].

Since accurate early diagnosis is the key to the effective long-term treatment and management of parkinsonism, we strongly support the early referral of all cases suspected of having parkinsonism for specialist assessment and advice.

Key points

- There is much misdiagnosis of both parkinsonism and Parkinson’s disease in subjects prescribed anti-parkinsonian drugs in general practice.
- One-quarter of subjects treated for Parkinson’s disease did not show any clinical evidence of parkinsonism.
- Common misdiagnoses were essential tremor, vascular pseudo-parkinsonism and Alzheimer’s disease.
- Validated clinical diagnostic criteria should be used to support the diagnosis of Parkinson’s disease.

References

13. Quinn N. Multiple system atrophy—the nature of the beast. J Neurol Neurosurg Psychiatry 1989; (Supplement): 78–89.
Appendix 1. UK Parkinson’s Disease Society Brain Bank clinical diagnostic criteria

Step 1. Diagnosis of Parkinsonian syndrome

Bradykinesia (slowness of initiation of voluntary movement with progressive reduction in speed and amplitude of repetitive actions) and at least one of the following:

(a) muscular rigidity
(b) 4–6 Hz rest tremor
(c) postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction

Step 2. Exclusion criteria for Parkinson’s disease

- History of repeated strokes with stepwise progression of parkinsonian features
- History of repeated head injury
- History of definite encephalitis
- Oculogyric crises
- Neuroleptic treatment at onset of symptoms
- More than one affected relative
- Sustained remission
- Strictly unilateral features after 3 years
- Supranuclear gaze palsy
- Cerebellar signs
- Early severe autonomic involvement
- Early severe dementia with disturbances of memory, language and praxis
- Babinski sign
- Presence of cerebral tumour or communicating hydrocephalus on computed tomography
- Negative response to large doses of levodopa (if malabsorption excluded)
- 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine exposure

Step 3. Supportive prospective positive criteria for Parkinson’s disease

(Three or more required for diagnosis of definite Parkinson’s disease)

- Unilateral onset
- Rest tremor present
- Progressive disorder
- Persistent asymmetry affecting the side of onset most
- Excellent response (70–100%) to levodopa
- Severe levodopa-induced chorea
- Levodopa response for 5 years or more
- Clinical course of 10 years or more