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USE OF THE LEVODOPA TEST IN THE ASSESSMENT OF PARKINSONISM ON A GERIATRIC INPATIENT UNIT

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Background: We studied prevalence of parkinsonism in patients admitted to an inpatient geriatric unit, factors associated with parkinsonism in this setting, and safety and validity of the levodopa test in geriatric inpatients with parkinsonism, many of whom have cerebrovascular disease or dementia.

Methods: The presence of parkinsonism was determined by a specialist in geriatric medicine for 850 consecutive geriatric inpatient unit admissions aged ≥65. The single-dose levodopa challenge was performed in 35 selected patients with parkinsonism.

Results: Of the 850 patients, 5% were labelled as having parkinsonism by other physicians, but did not meet study criteria for parkinsonism, 2% had parkinsonism that improved with discontinuation of neuroleptic medications on admission, 6.6% had ≥5-year history of drug-responsive parkinsonism felt to represent idiopathic Parkinson's disease, and 10.1% were felt to have 'new-onset parkinsonism' not related to current or previous neuroleptic medications. On multivariate analysis, cerebrovascular disease, dementia, and the absence of esophageal/peptic ulcer disease were all significantly and independently associated with 'new-onset parkinsonism' (p=.02, .02, and .001, respectively). 18 of 35 patients (51%) with 'new-onset parkinsonism' who were selected to undergo the levodopa test responded positively; there was no difference in likelihood of levodopa responsiveness between patients with and without cerebrovascular disease or dementia. At 1 month, all 18 patients who responded to levodopa continued chronic levodopa therapy with clinical improvement. Side-effects with single-dose levodopa were rare and relatively mild (transient nausea in 11% of patients).

Conclusion: Parkinsonism in geriatric inpatients is common, and is more likely to be associated with cerebrovascular disease and dementia than with idiopathic Parkinson's disease or previous neuroleptic medication exposure. The levodopa test for drug-responsive parkinsonism can safely and reliably be performed on a geriatric inpatient unit, is frequently positive in patients with cerebrovascular disease and dementia, and led to the initiation of chronic levodopa therapy in over 50% of selected patients.

Key words: Levodopa, Parkinson's disease, elderly, cerebrovascular disease, dementia

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INTRODUCTION

The incidence of both parkinsonism and Parkinson's disease increase steeply with increasing patient age.[1,2] Distinguishing parkinsonism from Parkinson's disease is difficult, and several autopsy studies have found misidentification rates of over 20%.[3-5] Well over 90% of patients with idiopathic Parkinson's disease have a good initial response to levodopa therapy, and previous studies have found that carefully measuring the response to a single levodopa dose accurately and safely predicts chronic levodopa responsiveness in newly diagnosed idiopathic Parkinson's Disease with a sensitivity of 75% and a specificity of 87%.[6-11] These studies have either focussed upon younger patients (average age <65 years), or excluded patients with other potential causes for parkinsonism, including cerebrovascular disease and dementia. The aims of our study were to: a) determine the prevalence of parkinsonism in patients admitted to an inpatient geriatric unit; b) assess the factors associated with parkinsonism in this setting; and c) determine the safety and validity of the levodopa test in assessing geriatric inpatients with parkinsonism, many of whom have cerebrovascular disease or dementia.

PATIENTS AND METHODS

A chart review of 1,009 consecutive admissions to the St. Joseph's Health Centre geriatric assessment unit in London, Ontario between March 1996 and May 2000 was undertaken, using a standardized chart extraction tool, which collected information on age, sex, presence of cerebrovascular disease, cardiovascular disease, dementia, dementia type, depression, benzodiazepene use, peptic ulcer disease, parkinsonism, and incontinence.

For all patients admitted to the geriatric inpatient unit, parkinsonism was defined according to the United Kingdom Parkinson's Disease Society Brain

Bank clinical diagnostic criteria (bradykinesia and at least one of muscular rigidity, 4-6 hz rest tremor, or postural instability not caused by primary visual, vestibular, cerebellar, or proprioceptive dysfunction).[12] A convenience sample of 35 patients with 'new-onset' parkinsonism not felt to be due to neuroleptic medication use or previously diagnosed idiopathic Parkinson's disease were studied further. To assess motor function, all sample patients completed 3 trials of the tap test ('tap your hand as many times as possible in 15 seconds between 2 pie plates 20 cm apart') and 3 trials of Timed up and go (TUG) test ('Stand, walk 3 metres, turn around, and come back, as quickly as is safely possible'). Patients then received 100 mg/25 mg of levodopa/carbidopa and 10 mg domperidone (to prevent levodopa-induced nausea and vomiting) orally. Three trials each of the tap test and TUG test were repeated 1 hour after administration of levodopa/carbidopa and domperidone. The mean of the 3 trials was taken at each stage; a positive levodopa response was defined as a 20% or greater improvement in either tap test or TUG test performance. Patients with a positive levodopa response were prescribed levodopa/carbidopa 100 mg/25 mg twice daily with domperidone 10 mg twice daily, with dosage adjustment at the discretion of the attending physician. All patients with a positive levodopa response were reassessed for continued response at 1 week and 1 month after levodopa initiation.

For all patients assessed, the diagnosis of dementia and dementia-type was made by the specialist in geriatric medicine providing ongoing care for the patient while in hospital on the geriatric inpatient unit. In most cases, results of a recent computerized tomography (CT) (61%) or magnetic resonance image (MRI) (12%) scan of the brain was available before discharge.

All statistical analyses were performed with SPSS software (version 9.0, SPSS, USA). The ability to predict 'new-onset' parkinsonism was examined using multivariate analysis.

RESULTS

Of 1,009 consecutive discharges, 51 were <65 years of age; discharge summaries were unavailable for 108 patients, leaving a sample of 850 patients. Of the patients, 42 (5%) were labelled as having parkinsonism by other physicians, but did not meet study criteria for parkinsonism. An additional 17 patients (2%) had parkinsonism that improved with discontinuation of neuroleptic medications at the time of admission to the geriatric inpatient unit. Of the patients, 6.6% (n=56) had a ≥5 year history of drug-responsive parkinsonism felt to represent idiopathic Parkinson's disease; in 3 of these patients, severe dysautonomia was present, suggestive of multiple-system atrophy. 'New-onset parkinsonism' not related to current or previous neuroleptic medication use was felt to be present in 10.1% of patients (n=86). The clinical and demographic features of patients with idiopathic Parkinson's disease, 'new-onset' parkinsonism, and the remaining geriatric inpatient unit population are shown in Table 1. In multivariate analysis, compared with the geriatric inpatient unit population as a whole, cerebrovascular disease, dementia, and the absence of esophageal/peptic ulcer disease were all significantly and independently associated with 'new-onset parkinsonism' (p=.02, .02, and .001, respectively).

Of the 35 selected patients with 'new-onset parkinsonism' who underwent the levodopa test, 18 responded positively to a single dose of levodopa (6 with a 20% or greater improvement in TUG time, 7 with a 20% or greater improvement on tap test, and 5 with a 20% or greater improvement on both tests). There was a mean improvement of 21% in tapping scores (range 0-50%) and 37% in TUG time (range 0-90%). In all 18 cases, improvements were maintained at 1 week and 1 month after the test. Side-effects with the levodopa test were rare and relatively mild (transient nausea in 11% of patients). Subsequently, 3 patients developed nausea and 1 patient developed hallucinations during their first month of levodopa therapy, necessitating levodopa dosage reduction.

The classification of patients with 'new-onset' parkinsonism, both those who did and did not undergo the levodopa test, is shown in Table 2. Vascular parkinsonism without dementia (n=17) and dementia with parkinsonism (n=57, the sum of rows 2 through 5 in Table 2) were more common than possible early Parkinson's disease or age-associated parkinsonism (n=12); however, there was no difference in the likelihood of levodopa responsiveness between patients with and without cerebrovascular disease or dementia. No statistically significant differences between responders and non-responders were found in any of the other clinical characteristics (Table 3).

Table 1. Descriptive Statistics

	General Geriatic Inpatient population (n=708)	'New-onset' Parkinsonism (n=86)	Idiopathic Parkinsons' Disease (n=56)	p
Sex (% female)	70%	65%	57%	0.01
Age (years)	80.7	79.0	77.6	0.03
% with cerebrovascular disease (coronary artery or peripheral vascular disease)	59%	63%	38%	0.01
% with hypertension	52%	42%	21%	0.02
Dementia	43.6%	66.3%	46.4%	0.01
Dementia Type:				0.01
Alzheimer's	16.8%	11.6%	7.1%	
Vascular	10.5%	22.1%	0%	
Mixed	12.0%	17.4%	0%	
Other	4.4%	15.1%	39.3%	
Peptic ulcer disease	36%	18.6%	19.6%	0.01
Depression	48.6%	46.5%	46.4%	NS
Incontinence	36.6%	44.2%	42.9%	NS
Urge incontinence	17.8%	22.1%	30.4%	0.04
% with previous neuroleptic exposure	10.4%	10.5%	14%	NS

DISCUSSION

Parkinsonism in elderly patients admitted to a geriatric inpatient unit is common, and is more likely to be associated with cerebrovascular disease and dementia than with idiopathic Parkinson's disease or previous neuroleptic medication exposure. Neither progressive supranuclear palsy nor corticobasal ganglionic degeneration were noted as causes for parkinsonism in our sample. The distribution of causes for parkinsonism in our sample is much more similar to that found in recent population studies[1,2] than in a neurology department,[10] while a recent study by Avorn et al[13] suggests that drug-induced parkinsonism may be the most common cause of parkinsonism in nursing home populations. The disproportionate representation of different causes for parkinsonism in these populations needs to be carefully considered in the interpretation of research findings.

The levodopa challenge test is a relatively quick and easy method to test for responsiveness to levodopa and can be performed relatively safely with elderly patients presenting with parkinsonism. The higher levodopa challenge response rate noted in our study (51%) compared with a previous study of patients with parkinsonism by Hughes et al[10] (20%) likely reflects differences in the underlying causes of parkinsonism in the two patient populations. Just as importantly, a negative single-dose levodopa challenge test should not be over-interpreted. A recent meta-analysis of 13 studies predominantly involving younger patients (average age 62.1 years) with parkinsonism suggests the sensitivity of the single-dose levodopa challenge test for the diagnosis of idiopathic Parkinson's disease is no better than 75%.[11] The sensitivity of the single-dose levodopa challenge test in patients with cerebrovascular disease and/or dementia is not known; a recent study would suggest use of a lower cut-off as a mea-

Table 2. Classification and Response to Levodopa Test in Patients with 'New-onset' Parkinsonism

Type	Positive Response	Negative Response	Levodopa Test Not Done	Total
Vascular parkinsonism without dementia	3	4	10	17
Vascular dementia	5	4	10	19
Mixed Alzheimer and vascular dementia	4	4	7	15
Lewy body dementia	3	2	8	13
Alzheimer dementia	0	2	8	10
Age-associated parkinsonism or early idiopathic Parkinson's disease	3	1	8	12
Total	18	17	51	86

Table 3. Clinical Characteristics of Levodopa Test Responders versus Non-responders

	Levodopa test responders (n=18)	Levodopa test non-responders (n=17)
sex (% female)	72%	53%
age (years)	80.6	80.1
% with cerebrovascular disease	67%	70%
% with other coronary artery or peripheral vascular disease	33%	53%
% with hypertension	40%	47%
% with dementia	67%	70%
% with depression	44%	24%
% with incontinence	39%	53%
% with upper GI disease	11%	29%

sure of response to single-dose levodopa (14% improvement instead of 20% improvement) provides a more accurate prediction of response to chronic levodopa treatment.[14] The existence of a long duration response to levodopa in idiopathic Parkinson's disease, which takes days to appear and days to disappear, is well-documented, and may be an important confounding factor in the interpretation of levodopa challenge test results in patients with parkinsonism not felt to be due to idiopathic Parkinson's disease.[15,16] Although the need for intravenous administration makes the use of one-day apomorphine testing unwieldy in frail elderly patients with parkinsonism, there is increasing evidence that dopamine agonists such as lisuride and ropinirole may be well-tolerated and useful in assessing parkinsonism in the elderly.[17]

Larger studies are needed to confirm the long-term clinical usefulness and tolerability of levodopa in elderly patients with parkinsonism due to strokes and dementia. Until further data is available, a history of cerebrovascular disease or dementia in an elderly person with parkinsonism should not preclude a levodopa challenge test to determine drug responsiveness.

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