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ScienceDirect
Journal of Clinical Neuroscience 16 (2009) 246–252
Journal of Clinical Neuroscience
www.elsevier.com/locate/jocn

Clinical Study

Impact of dopamine transporter single photon emission computed tomography imaging using I-123 ioflupane on diagnoses of patients with parkinsonian syndromes

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Received 20 September 2007; accepted 21 January 2008

Abstract

To assess the impact of I-123 ioflupane single photon emission computed tomography (SPECT) imaging on classifying patients with striatal dopaminergic deficits. Sixty-one patients with an initial diagnosis of parkinsonism or uncertain tremor disorder were screened and followed-up for one year. All patients were re-examined by two neurologists at our centre and were classified as having neurodegenerative or non-neurodegenerative disorders. Patients underwent I-123 ioflupane SPECT imaging. SPECT studies were blindly evaluated and classified as normal or abnormal (indicative of neurodegenerative disorders). The overall agreement of the SPECT imaging results with the initial classification was 65.6% (kappa = 0.229, $p = 0.074$) but was 90.2% (kappa = 0.782, $p < 0.001$) with the classification of the neurologists at our centre. I-123 ioflupane SPECT imaging is a valuable method in the evaluation of patients presenting clinically with uncertain parkinsonian syndromes or for whom diagnostic doubt exists.

Keywords: Dopamine transporter; Parkinsonism; SPECT; 123I-ioflupane

1. Introduction

The diagnosis of parkinsonism is currently based on clinical evaluation, although the clinical signs may be related to a neurodegenerative disorder such as Parkinson's disease (PD), progressive supranuclear palsy or multiple system atrophy.[1] However, subtle parkinsonian signs are common in elderly patients with non-neurodegenerative disorders such as essential tremor.[2]

In general practice the presence of parkinsonism is misdiagnosed in up to a quarter of cases. According to Hughes et al., movement disorder specialists misdiagnose parkinsonian syndromes in up to 10% of cases. Histopathological findings are the "gold standard", and the highest accuracy of PD diagnosis using the current clinical criteria is about 90%.[3,4] In another report, experienced neurologists were found to have altered their diagnosis in 36% to 54% of cases following the first evaluation.[5] Additionally, in a considerable number of clinicopathological studies, a significant percentage of patients (10–25%) with an antemortem clinical diagnosis of PD were found to have other diseases in a post-mortem evaluation.[6,7]

Although the differential diagnosis of PD from essential tremor or other parkinsonian syndromes is relatively straightforward according to the United Kingdom Parkinson's

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0967-5868/$ - see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.jocn.2008.01.020

Disease Society Brain Bank criteria, the diagnosis may be difficult in elderly patients or when the disorder is at an early stage and a false diagnosis is possible.[8–13]

Therefore, new techniques to further improve the accuracy of diagnosing PD and other neurodegenerative parkinsonian syndromes early in the clinical course would be important and valuable tools for the clinician.

Dopamine transporter (DAT) is expressed exclusively on the presynaptic terminals of dopaminergic neurons. Degeneration of these terminals is accelerated in neurodegenerative parkinsonism, resulting in a reduction of the numbers of dopamine transporters. Imaging of presynaptic dopaminergic neurotransmission using radionuclide studies has become of significant clinical importance, not only for the objective confirmation of presynaptic nigrostriatal degeneration, but also for the early differential diagnosis of PD from non-neurodegenerative disorders.[5]

Several radiopharmaceuticals that have been developed for single photon emission computed tomography (SPECT) imaging can be used as sensitive and objective presynaptic dopaminergic markers. Among them, I-123 ioflupane (I-123 FP-CIT, DaTSCAN, General Electric Healthcare Division, Buckinghamshire, UK) is one of the most promising radiotracers, as it has favourable pharmacokinetic properties which allow imaging 3–6 hours post injection.[14] SPECT imaging using I-123 ioflupane can accurately differentiate parkinsonian syndromes.[5,15]

The aim of the present study was to assess the impact of I-123 ioflupane SPECT imaging on the classification of patients with striatal dopaminergic deficits and to evaluate its clinical application by the neurologists.

2. Methods

2.1. Patients

A total of 83 patients underwent a screening evaluation, of whom 22 patients were excluded (13 refused to sign the informed consent form and 9 were excluded because they did not fulfil the enrolment criteria). Finally, 61 Caucasian patients, aged 64.73 ± 13.60 years, were enrolled in the study, who had a mean duration of diagnosed illness of 4.36 ± 3.76 years (demographic and drug therapy data are summarised in Table 1). Twenty healthy volunteers were evaluated in order to obtain reference SPECT data. The mean age of control subjects was 63.33 ± 19.01 years ($p = 0.762$ compared to the patients) (Table 1).

Table 1
Characteristics of the study group

	Patients	Controls
Age (years)	64.73 ± 13.60	63.33 ± 19.01
Percentage men	60.65	64.2
Symptom duration (years)		
Neurodegenerative	3.2 ± 2.8	
Non-neurodegenerative	7.2 ± 4.7	

Study subjects were recruited from consecutive patients admitted to our outpatient clinic. Eligible for recruitment were those with a presumed diagnosis of a parkinsonian extrapyramidal or tremor disorder. Patients who were diagnosed as having a "parkinsonian syndrome" by their treating community neurologist (with no special training in extrapyramidal disorders) presented with at least two of the following motor signs: rest tremor, bradykinesia or rigidity. All patients (40 in total) with a diagnosis of neurodegenerative disorder were taking PD medication (Table 2), 32 of whom exhibited a satisfactory therapeutic response. Patients with iodine allergy were excluded. Other exclusion criteria were pregnancy, serious comorbidities, use of drugs that bind to the dopamine transporter, structural damage to the basal ganglia as visualised in CT scans or MRI, and a history of exposure to manganese.

2.2. Study design

The study was a prospective trial. It was conducted with the approval of the institution's ethics committee in accordance with the Helsinki Declaration. Eighty-three consecutive patients were screened. All patients who agreed to enrol in the study signed a consent form and they were classified into two groups. The first group consisted of patients with an initial diagnosis of a neurodegenerative parkinsonian disorder (A1) and the second group consisted of patients with an initial diagnosis of a non-neurodegenerative disorder (A2). Every patient was re-examined, using the established diagnostic criteria, by our centre's experienced neurologists (CB [examiner 1] and IP [examiner 2]), who were blinded to the initial diagnosis.[8,16–18]

The examiners at our centre used only clinical criteria, without using any other diagnostic test (such as the smell test), as neuroimaging was performed before enrolment.[7] After the patients were examined their drug therapy was altered in accordance with the final diagnosis and the patients were followed up for one year. We believe this

Table 2
Diagnoses at enrolment and by our neurologists

Type of neurodegenerative disorder	No. patients	Type of non-neurodegenerative disorder	No. patients
Diagnosis at enrolment			
Parkinson's disease	35	Essential tremor	15
Progressive supranuclear palsy	3	Uncertain tremor disorder	3
		Vascular parkinsonism	2
Multiple system atrophy	2	Psychogenic	1
Total	40	Total	21
Diagnosis by neorologists at our centre			
Parkinson's disease	34	Essential tremor	15
Progressive supranuclear palsy	3	Cerebellar disorder	3
		Vascular parkinsonism	3
Multiple system atrophy	2	Drug-induced parkinsonism	1
Total	39	Total	22