

ORIGINAL ARTICLE

Clinical impact of DaTSCAN: a 5-year review

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Abstract

Aims The clinical diagnosis of idiopathic Parkinson's disease (IPD) and its associated parkinsonian syndromes is not simple as it can be mimicked by a variety of other conditions. Objective assessment of the dopamine transport (DAT) system by ^{123}I-Ioflupane SPECT has proven to be a highly accurate method for establishing a diagnosis of IDP. However, the test is expensive and can only be justified if it can lead to a change in patient management. This retrospective study therefore aimed to determine the clinical impact of ^{123}I-Ioflupane SPECT scan in our Institute.

Methods A retrospective review of the clinical impact of ^{123}I-Ioflupane imaging in a single University Hospital site over a 5-year period was undertaken. Of the total of 152 patients imaged, follow-up information was available in 85 of the patients who presented with either a high pre-test probability of IPD (43 patients), or unlikely to have IPD (15 patients) or atypical movement disorders (27 patients).

Results In those patients in whom a diagnosis of IPD was suspected, the scan confirmed the disease in 79%, with a change in management in 23. In those with a low likelihood of IPD, 33% had a diagnostic ^{123}I-Ioflupane scan suggestive of IPD, with resultant change in management in 20% of patients. Of those with atypical presentation, IPD was confirmed in 48%, all of whom had a change in management.

Conclusion In conclusion, there was a 64% agreement between the clinical diagnosis and imaging, resulting in a change in management in 28 percent of the patients.

Key words: *Parkinson syndrome, I-123 Ioflupane, SPECT quantification*

Introduction

The accurate diagnosis of idiopathic Parkinson's disease (IPD) is important because of its significant implications for both diagnosis and treatment. The clinical diagnosis of IPD is not always accurate, with clinicopathological studies reporting a high error rate at 24% [1]. CT and MRI imaging have a limited use in IPD, and are mainly restricted to excluding other causes for the symptoms, such as vascular insults and tumour.

The role of functional imaging of the basal ganglia utilising the dopamine transporter (DAT) system has become more important. DAT is a sodium-chloride dependent protein on the pre-synaptic dopaminergic nerve terminal

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that controls the dopamine levels by active reuptake of dopamine after its interaction with the postsynaptic receptor [2]. ^{123}I-Ioflupane, a cocaine derivative with no pharmacological action on the dopamine system, is the only commercially available ligand, which can be used to identify the DAT system in vivo. In a series of studies, the technique has been shown to deliver highly accurate studies delivering both a positive and negative predictive value of more than 90% [3].

Although the ^{123}I-Iopflupane SPECT scan has a high level of accuracy, it is an expensive test costing at least US$1100 (€850), and hence there is a need to justify its use in the clinical setting. This review was therefore performed in order to determine the frequency of the alteration in patient management on the basis of ^{123}I-Ioflupane scintigraphy results.

Methods

A retrospective review of the use of ^{123}I-Ioflupane was performed using a list of all the patients who have undergone such scanning at a single nuclear medicine department over a 5-year period in a University Hospital with a neurology department which has a specialist interest in movement disorders. Patients were referred from surrounding hospitals and community health units covering a population of approximately 2 million. The information was obtained from the radiology information system (RIS). A total of 152 patients were identified as having a ^{123}I-Ioflupane study during the study period. An attempt was made to identify medical records from all referring units sending patients for imaging. This included one of the researchers (BYW) travelling out to each of the referral sites.

Information was available from 85 patients, the main reasons for failure to collect information included lost records, records sent to other health providers, a record not available and the patient's death. Using a combination of the questionnaire to the referring physician, the review of the medical notes, the pre-scan diagnosis was made and the patients were placed into one of three groups:

Group 1: Pre-scan clinical diagnosis of likely to be IPD (includes idiopathic Parkinson's Disease, multi system atrophy and progressive supranuclear palsy)

Group 2: Pre-scan clinical diagnosis unlikely to be IPD (e.g. akinetic rigid syndrome, corticobasal degeneration, essential tremor, etc.)

Group 3: Pre-scan diagnosis unclear

Then in each of these three groups by using the results of the ^{123}I-Ioflupane study, the information provided by the referring clinician and the medical notes. The following two parameters were defined:

1. Was the clinical diagnosis after the scan the same as the pre-scan diagnosis or did the scan result in a change of diagnosis?

2. Did the result of the ^{123}I-Ioflupane study alter the patient's management, for example, by a starting or stopping or changing the use of anti-parkinsonian drugs?

The audit used the results of the clinical report, which in our Institute follows Catafou's abnormality criteria and grading (Figure 1) [3].

Results

Group 1

In the group 1, 43 patients were identified, 25 males and 18 females, with a mean age of 58 years (range 19-83).

Clinical diagnosis correlated with a positive 123I-Ioflupane scan diagnosing IPD in 34 (79%) patients (Figures 2-4). Of these 25 had been started on anti-parkinsonian medication prior to scan (74%). In the 9

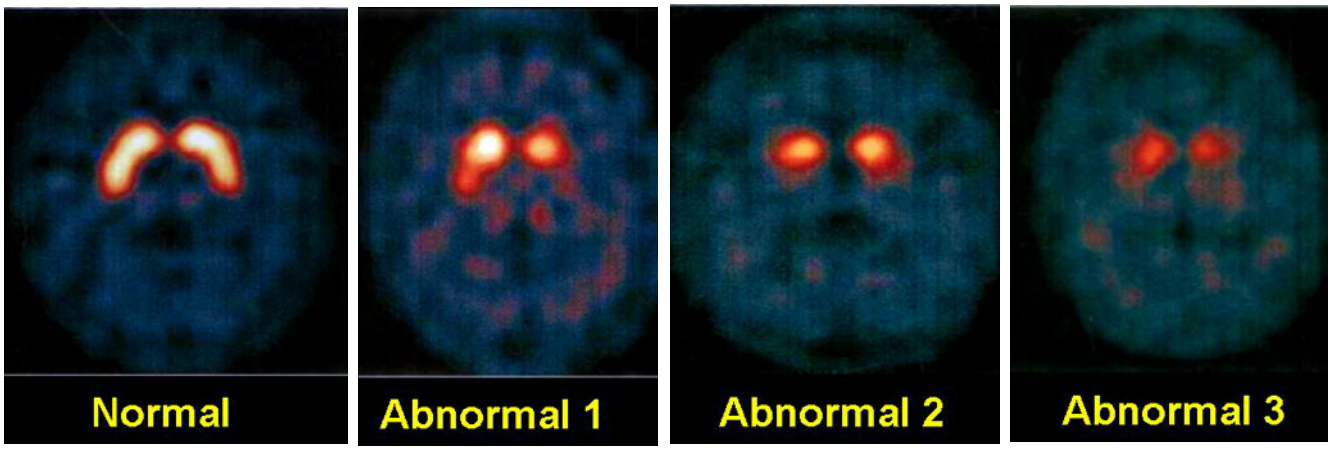

Figure 1 *Series of images showing increasingly abnormal uptake of ^{123}I-Iopflupane in the basal ganglia from left to right: normal, abnormal stage 1, abnormal stage 2 and abnormal stage 3*

patients who had not received anti-parkinsonian drugs before the ^{123}I-Ioflupane scan; all patients were subsequently started on these drugs post-scan (100%).

There were nine patients with a normal ^{123}I-Ioflupane scan (21%), of whom four had been started on anti-parkinsonian medication prior to the ^{123}I-Ioflupane study (44%). Of these 4, only 1 had their anti-parkinsonian medication stopped; a further patient had anti-parkinsonian medication started despite the normal scan. Of the 14 patients who were not started on anti-parkinsonian medication prior to the 123I-Ioflupane scan, 9 had a positive scan (64%). All 9 were subsequently started on anti-parkinsonian medication as part of their management.

Out of the 13 patients who should have had their management changed after the ^{123}I-Ioflupane scan in this group (either the start or stop anti-parkinson medication), only 10

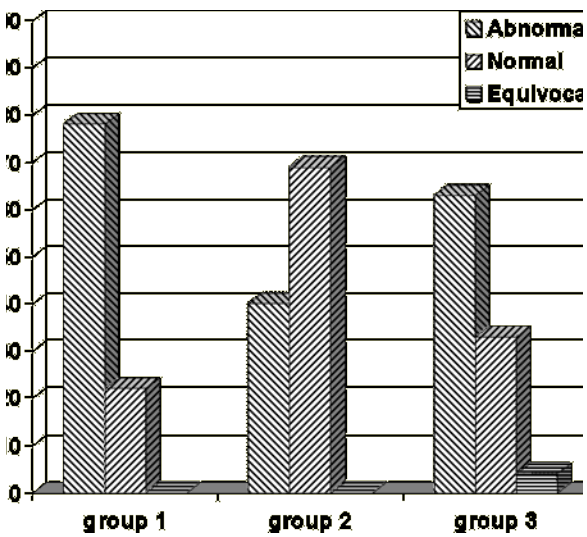

Figure 2 *Abnormal, normal and equivocal scan results by group*

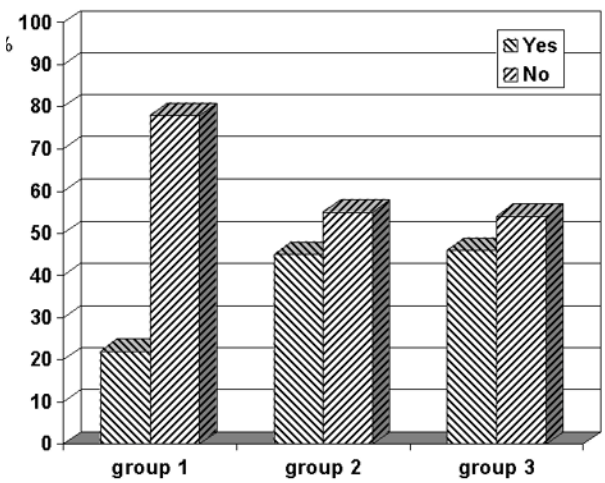

Figure 3 *Agreement between clinical diagnosis and ^{123}I-Iopflupane by group*

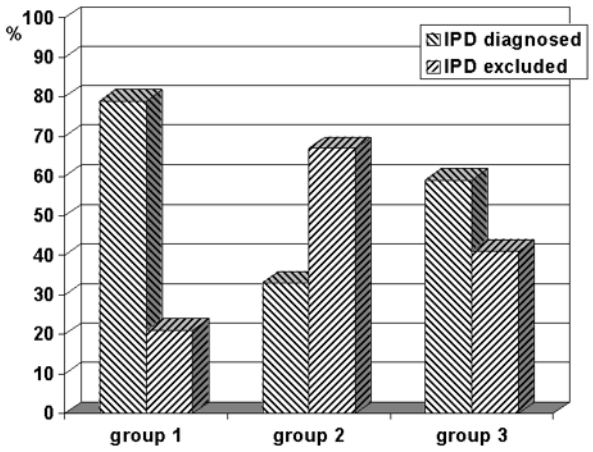

Figure 4 *Diagnosis following ^{123}I-Iopflupane SPECT by group*

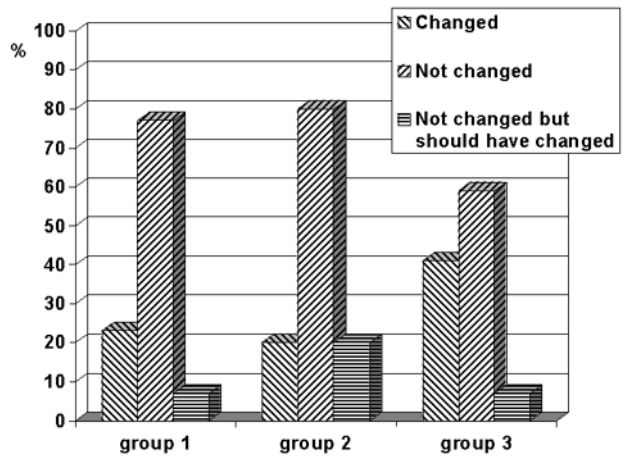

Figure 5 *Change in management following ^{123}I-Iopflupane by group. In addition is displayed the percentage of patients in each group that should have had a change of management but did not. (Note: The numbers for each of the groups 1, 2 and 3 add up to more than 100%)*

had such a change initiated. Therefore, the ^{123}I-Ioflupane scan results, changed the management in 77% of patients in whom it should have made a difference and in 23% overall in this group (Figure 5).

Group 2

There were 15 patients in Group 2 (9 male, 6 female) with a mean age of 59 years (range 29-76). Five patients had a positive ^{123}I-Ioflupane scan consistent with IPD (33%). Of the remaining, nine patients had a normal ^{123}I-Iopflupane scan (60%), though one patient had an abnormal ^{123}I-Ioflupane but due to marked asymmetry, the scan was reported as likely to be due to a vascular cause and not IPD (7%).

There were five patients who had anti-parkinsonian medication prescribed prior to the ^{123}I-Ioflupane scan, 3 of whom had a normal scan and 1 of these (33%) had their medication stopped whilst the other 2 continued their medication.

There were 10 patients who did not have anti-parkinsonian medications prescribed prior to scan - of these, 3 turned out to have a positive ^{123}I-Ioflupane scan consistent with IPD (30%), and subsequently 2 (67%) had anti-parkinsonian medication commenced; medication was deferred in the remaining patient as it was felt the clinical symptoms were not sufficient to warrant starting medication at the time of the scan report. Only 3/6 (50%) of patients, who should have had their management changed by the ^{123}I-Ioflupane scan, actually did (Figure 5). The clinical diagnosis was taken to be correct in anyone started on anti-parkinsonian medi cation prior to scan and who had a positive ^{123}I-Ioflupane scan (2 patients), and also in those not taking medication with a negative scan (5 patients). The clinical diagnosis was correct in seven (47%) patients (Figure 3).

Group 3

In group 3, there were 27 patients including 11 males and 16 females (mean age = 67 -range 31 - 89). Of these 16 patients had a positive ^{123}I-Ioflupane consistent with IPD (59%), 9 had a normal study (33%), and in one patient with a positive scan, the study was reported as equivocal due to appearances suggestive of a vascular cause (4%) and (4%)

(Figure 2). There were 12 patients in this group that had been started on anti-parkinsonian medication prior to scan (44.4%). Of these, 4 had a normal ^{123}I-Ioflupane scan and in one patient, the scan was equivocal. Three of these patients with normal scans had their anti-parkinsonian medications stopped (75%). Of the 15 patients who did not have anti-parkinsonian medication prior to scan, 9 turned out to have a positive ^{123}I-Iopflupane study consistent with IPD (60%) and 8 of these had anti-parkinsonian medication commenced (89%). Therefore, 11/13 (85%) patients should have had their management changed in this group after their ^{123}I-Iopflupane study (Figure 5). When we compared the pre-study clinical diagnosis it was correct in only 13 (48%) patients (Figure 3).

When looking at the results overall, there was agreement between the clinical diagnosis in 54/85 patients (64%). In 24/85 (28%) patients, the clinical management was changed, giving an overall cost of US$3600 (€2600) per corrected diagnosis.

Discussion

The results of this study confirm that the clinical diagnosis of IPD is only correct in about 2/3 of all patients, which is less than what would be expected from correlation of clinical findings and pathology [1]. Even where a diagnosis appears to be of a high probability clinically, 21% of patients had a normal study. This has been found in many centres, and in a recent multicentric trial of 99 patients across

Europe, it was found that 44% of the patients with a clinical diagnosis of IPD, had a normal study [5]. It is also a worrying finding considering the fact that IPD probably represents the most common neuro-degenerative movement disorder [6-8]. The incidence of IPD is considered to be variable, but 100 cases per 100,000 would seem to be the average in Europe [7, 8]. It would mean that a country with a population of 100 million would have 100,000 cases, of which only 67,000 would be correctly diagnosed.

This reflects a significant burden of disease that would be mismanaged, and whilst the parkinsonian syndromes are thought of as a disease of the elderly, a significant proportion of sufferers, especially those with the early form of disease, may be much younger, with the onset of symptoms before 30 [9]. Therefore, there is the potential for patients to suffer many years of misdiagnosis and maybe mismanagement. Though, the cost of the test is high, the economic cost of the subsequent disability for undiagnosed and mismanaged IPD is also high [10, 11].

Other studies have confirmed that ^{123}I-Ioflupane imaging changes clinical management in a significant proportion of patients [2, 3, 5, 12]. However, the fact that in some patient groups, up to 75% of all the patients with an initially incorrect diagnosis, had a resultant change in the drug regime, suggests that the results of the ^{123}I-Ioflupane study are pivotal in influencing the clinicians on how to treat this patient group.

Unsurprisingly, the least change in management was seen in the group of patients where the diagnosis of IPD was considered likely when the scan was performed for confirmatory purposes. In those patients where the pre-scan diagnosis was unclear or unlikely to be due to IPD, the biggest change of management was achieved - in about 50% of those imaged.

Therefore it seems that this expensive imaging technique should be used where there is real doubt about the diagnosis and not just to confirm clinically suspicious findings. The cost of anti-parkinsonian treatment is seen as small in one area of Scotland covering about 100,000 people with 610 receiving medication for IPD. However, on subsequent investigation including ^{123}I-Ioflupane imaging, a five percent misdiagnosis rate was found, with the average duration of unnecessary treatment being seven years, resulting in a cost burden of €150,000 per annum on useless medication [13].

Conclusion

Our study shows that in 36% of cases, ^{123}I-Ioflupane scanning provided information not available clinically and subsequently changed patient management in 28% of the cases. The greatest contribution of ^{123}I-Ioflupane was made in those patients in whom there was diagnostic uncertainty pre-scan but ^{123}I-Ioflupane can be useful in any patient with a suspected Parkinson's disease. However, 10% of patients should have had their medication changed following the ^{123}I-Ioflupane study but did not. (Fig 5). Therefore, it appears that further education of the referring clinicians concerning this test may be required.

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