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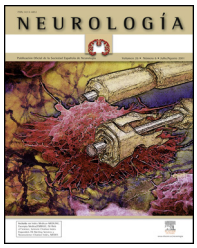

ORIGINAL ARTICLE

Longitudinal evaluation using FP-CIT in patients with parkinsonism☆

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KEYWORDS
I123-Ioflupane;
Dopamine transporters;
Parkinsonism;
False negatives

Abstract
Objective: To assess a group of patients with parkinsonism using serial studies with FP-CIT, basically the initial false negative results.
Methods: Restrospective study of 92 patients (55 men and 37 women) who had undergone 2 different FP-CIT studies because of discrepancies between study results and clinical progression. The mean elapsed time between the studies was 26 months (SD: 6). We performed a semi-quantitative study using the patient's clinical history and the available literature to analyse discrepant cases with a normal initial study and subsequent pathological findings.
Results: A total of 184 studies were completed for 92 patients; 11 of those 92 showed discrepancies between initial and subsequent studies. Among the 11 discrepant cases, 7 showed a normal initial study and pathological findings at a later date. Analysis of the predominant clinical features that might explain this behaviour revealed that 4 of these 7 subjects presented tremor-dominant parkinsonism. Regarding the rest, 1 presented early stage parkinsonism and was treated with antidopaminergic agents; 1 was classified as probable multisystem atrophy type C, and the third showed clinical signs of atypical parkinsonism without any causes of those signs being identified.
Conclusions: Serial FP-CIT studies are unnecessary in the large majority of cases, but they may be justifiable in certain clinical situations.

PALABRAS CLAVE
I123-Ioflupano;
Transportadores de dopamina;

Evaluación longitudinal con FP-CIT en pacientes con parkinsonismo

Resumen
Objetivo: Analizar un grupo de pacientes con síndrome parkinsoniano mediante estudios seriados con FP-CIT, valorando fundamentalmente los resultados falsamente negativos iniciales.

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Parkinsonismo;
Falsos negativos

Métodos: Estudio retrospectivo en el que se incluye a 92 pacientes (55 varones y 37 mujeres), a los que se les realizó un doble estudio con FP-CIT pues existían discrepancias entre este y la evolución clínica del paciente. El tiempo medio ± desviación estándar transcurrido entre ambos estudios fue de 26 ± 6 meses. Se realizó una valoración semicuantitativa analizando mediante la historia clínica y la bibliografía disponible los casos discrepantes con estudio inicial normal y posterior patológico.
Resultados: Del total de 184 estudios realizados a 92 pacientes, 11/92 mostraron resultados discrepantes entre estudio inicial y tardío. De estos, en 7/11 el estudio inicial fue normal y el posterior patológico. Los rasgos clínicos predominantes que pudieran explicar este comportamiento mostraron que en 4/7 sujetos destacó la presentación de un cuadro parkinsoniano con predominio de la clínica tremórica; 1/7 presentó un síndrome parkinsoniano en estadio inicial en tratamiento con fármaco antidopaminérgico, 1/7 fue catalogado de probable atrofia multisistema tipo C y 1/7 presentaba un cuadro de parkinsonismo atípico, sin que encontráramos justificación para dicho comportamiento.
Conclusiones: La realización de estudios seriados con FP-CIT carece de fundamento en gran proporción de casos, aunque existen ciertas situaciones clínicas que pueden justificarlo.

Introduction

Dopamine transporters (DAT) are proteins in the presynaptic terminal of dopaminergic neurons which are responsible for dopamine re-uptake. DAT density measurement, by means of SPECT or PET tomographic techniques using specific ligands, provides a direct in vivo measurement of the integrity of the striatonigral pathway. Several tracers derived from tropane and cocaine analogues, such as ioflupane or 123I-FP-CIT (N-ω-fluoropropyl-2ß-carbomethoxy-3ß-[4-iodophenyl] nortropane), have been used for these measurements. This diagnostic technique allows doctors to detect Parkinson's disease (PD) even during its premotor phase, such as in cases of olfactory deficit[1] or REM sleep behaviour disorder.[2] It has been determined that in cases of loss of dopaminergic neurons, DOPA decarboxylase is up-regulated[3] while DAT receptors are down-regulated.[4] In theory, this situation contributes to a high level of sensitivity. Results from SWEDD patients (Scan Without Evidence of Dopaminergic Deficit), a group accounting for 10% of the patient total according to data from different clinical studies on neuroprotective drugs, will decrease the diagnostic validity of the technique. Even after taking the presence of these patients into account, the test's negative predictive value does not reach optimal values.[5]

Annual loss of dopaminergic neurons from the nigrostriatal pathway in patients with degenerative parkinsonism (PK) has been estimated at 6% to 13%[6] compared to the 0% to 2.5% change per decade measured in age-matched healthy controls. The rate of progression is not linear and loss is more rapid during initial stages than in advanced stages. For the above reasons, it seems logical to perform a new study after a reasonable period of time in order to assess the progression of a case of degenerative PK.

This study aims to analyse a group of patients with parkinsonian syndrome (PS) who underwent serial studies with FP-CIT scans. We mainly focused on those patients with an initial evaluation classified as normal (N) and a subsequent scan classified as pathological (P) (N—P sequence). By analysing each patient's clinical history and available literature, we aim to determine the most probable causes of such a pattern as a source of potential false negative results. In the same way and as a secondary aim, we also evaluated the inverse sequence (P—N).

Materials and methods

Patients

We retrospectively studied 92 patients (55 men and 37 women) from our hospital's movement disorders unit. We performed two serial FP-CIT scans on each patient, one at baseline and the other at a later point to investigate discrepancies between initial scan results and the patient's clinical symptoms. We also included 20 patients with a clinical diagnosis of essential tremor as control subjects after a preliminary analysis.

The final clinical diagnosis was established after a minimum follow-up of 18 months for patients in our main study group (those with contradictory scan results). All patients were in a similar stage of the disease since doctors had requested a FP-CIT scan after the initial clinical evaluation in all cases. Table 1 shows the breakdown of patients according to the first provisional diagnosis.

Mean time ± standard deviation elapsed between the two studies was 26 ± 5 months. The mean age of the patients when the initial study was performed was 69.3 years (range, 36—84) with a standard deviation of 9.2 years.

Method

Images were captured 3 to 4 hours after intravenous injection of 185 MBq (5 mCi) of 123I-FP-CIT. Lugol solution had previously been administered to achieve thyroid