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Psychiatric Manifestations Secondary to the use of a Dopaminergic Agonist Antiparkinsonian: A Case Report

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Abstract **Case Report**

Psychiatric disorders in Parkinson's disease can be classified into two opposing categories: hypodopaminergic if related to dopaminergic denervation and hyperdopaminergic if related to dopaminergic treatment. In this context the aim of this clinical case study is to present the psychiatric manifestations due to the use of a dopaminergic agonist anti parkinsonian (piribedil). We report the clinical case of a 55-year-old patient, hypertensive on Amlodipine, suffering from a parkinsonian disorder for 4 years; presenting to the psychiatric consultation at Ibn Nafis Hospital for a behavioural disorder following the introduction of Piribedil (antiparkinsonian dopaminergic agonist). Most of the psychic side effects of antiparkinsonian drugs are linked to their central dopaminergic properties. These effects are secondary to excessive stimulation of mesocorticolimbic dopamine receptors and/or serotonin hyperactivity.

Keywords: Psychiatric disorders, psychiatric consultation, hyperdopaminergic, behavioural disorder.

1. INTRODUCTION

The psychological disorders of Parkinson's disease can be classified in two opposing categories:

- Hypodopaminergic if they are related to dopaminergic denervation (apathy, depressive disorder, anxiety, sleep disorders, concentration disorders, eating disorders....)
- Hyperdopaminergic if they are related to dopaminergic treatment (hallucinations, delusions, pathological gambling, compulsive shopping, hypersexuality...)

In this context we propose the study of a clinical case presenting the psychiatric manifestations due to the use of a dopaminergic agonist anti Parkinson

2. CASE CLINIQUE: OBSERVATION

A 55-year-old man with hypertension on Amlodipine was diagnosed with Parkinson's disease a few months after the onset of right unilateral tremor in 2018.

He was treated with PIRIBEDIL (TRIVASTAL*: dopaminergic agonist) 50 mg/d + Artane (trihexyphenidyl) 2.5 mg/d.

Over the next four years, the disease progressed towards an akineto-rigid parkinsonian syndrome that sometimes-impaired mobility.

The patient benefited from an increase in the dose of the dopaminergic agonist (300 mg/d of Piribedil).

Two months later, the patient presented to the psychiatric emergency department at Ibn Nafis Hospital accompanied by his family for a behavioural disorder consisting of:

- Psychomotor agitation seizures.
- Persecutory delusions with an interpretative mechanism.
- Hallucinatory syndrome (HV and HA).
- Irritability or even aggressiveness.
- Insomnia on falling asleep with multiple awakenings.
- Sad mood with two suicide attempts.
- Notion of setting fires.

Taking Charge:

- An organic work-up was carried out and came back without any particularity.
- Symptomatic antipsychotic treatment (Risperidone 1 mg/d, gradually increased to 2 mg/d) was started.

- A neurological consultation was carried out to adjust the anti-parkinsonian treatment: Piribedil was withdrawn and Trivastal° (dopaminergic agonist) + L-Dopa was introduced.
- A complete clean-up was observed after 15 days.
- Antipsychotic treatment was stopped after two months.

3. DISCUSSION

Parkinson's disease is the result of a dopamine deficit in the nigrostriatal region. The principle of its treatment is based on compensating for the dopaminergic deficit through various pharmacological means:

1) By supplying exogenous L-dopa, which is taken up by the brain's dopaminergic neurons and converted into dopamine,
2) By mimicking the action of dopamine on dopamine receptors through the use of dopamine agonists, which act directly on post-synaptic D2 dopamine receptors and therefore require neither conversion nor metabolism in the dopamine neurons,
3) By inhibiting the enzymes involved in dopamine catabolism, such as COMT or MAO-B, in order to limit its degradation.

Dopamine substitution has led to an improvement in the parkinsonian triad [1,2].

Most of the psychic side effects of antiparkinsonian drugs are related to their central dopaminergic properties.

These effects are secondary to excessive stimulation of mesocorticolimbic dopamine receptors and/or serotonin hyperactivity.

Various risk factors have been identified:

- Gender: men are more likely than women to suffer from these psychological symptoms.
- Age: most patients have had PD for a long time and it started at an early age
- A history of depression and/or addiction are common in patients suffering from the troublesome psychological effects secondary to Dopa therapy
- A possible genetic predisposition to D2, D3 or D4 receptors;

lastly, and most importantly, treatment with dopaminergic agonists: it has been found that patients suffering from dopaminergic dysregulation syndrome with psychic manifestations receive a higher dose of dopaminergic agonists [3], which is consistent with our case.

The psychotropic effects of dopa therapy have been described in Parkinson's disease: a change in personality with an "awakening" effect, an elation of mood, a "carefree attitude", an improvement in apathy, an increase in libido, a reduced need for sleep, more rarely hallucinations and psychosis [4, 5, 6].

The prevalence of psychosis has been estimated at 13% [7], occurring mainly in patients with cognitive impairment.

Damage to the mesocorticolimbic system in Parkinson's disease [8] could explain the pathophysiological mechanisms of these non-motor disorders, secondary to dopaminergic denervation, and the non-motor complications of dopaminergic treatment, explained by hypersensitivity of mesocorticolimbic dopaminergic receptors [9].

The appearance of dopaminergic agonists in the 1970s was an important step.

They are less powerful than L-dopa at the motor level, causing fewer dyskinesias [10], but are more active at the non-motor level, with an antidepressant [11] and antipathic effect [12]. However, this also increases the risk of neuropsychiatric side-effects.

Psychosis and mania were the first to be described [4], with a higher risk in elderly patients with less cognitive and behavioural "reserve".

Dopaminergic agonists are now prescribed as first-line treatment for young parkinsonian patients to reduce the risk of dyskinesias [13].

Certain behaviours, such as pathological gambling, compulsive buying and hypersexuality, have been mainly associated with dopaminergic agonists [14].

Pathological gambling, hypersexuality and compulsive buying are the most frequent and the most serious [15, 16]. The lifetime prevalence of these three behavioural disorders combined is 6.1%, rising to 13.7% in Parkinson's patients treated with dopamine agonists [14].

The scale of these figures and recent discoveries clearly illustrates the importance of systematically assessing psychological and behavioural aspects in the management of patients with Parkinson's disease.

4. CONCLUSION

Parkinson's disease is the most common neurodegenerative disease, after Alzheimer's-type dementia. Dopaminergic therapy plays a fundamental role in its treatment.

Dopaminergic agonists can have psychological side-effects, which should be systematically investigated.

Treatment involves adapting dopaminergic therapy as well as the use of psychotropic drugs (antidepressants, mood regulators, atypical neuroleptics).

Early assessment of the disorders and patient follow-up are crucial points in the multidisciplinary management of their effects.

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