Journal Homepage: -www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI:10.21474/IJAR01/15221
DOI URL: http://dx.doi.org/10.21474/IJAR01/15221

*RESEARCH ARTICLE*

# PSYCHOTIC SYMPTOMS AND PARKINSON'S DISEASE: CLINICAL AND THERAPEUTIC ASPECTS

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## Manuscript Info

***Manuscript History***
Received: 18 June 2022
Final Accepted: 22 July 2022
Published: August 2022

***Key words:-***
Psychosis, Parkinson's Disease, Symptoms, Therapeutic

## Abstract

**Introduction:** Parkinson's disease (PD), the second most common neurodegenerative disease after Alzheimer's disease. Affects 1% of the population after the age of 60. Motor symptoms are the most common features that may be associated with non-motor symptoms including psychotic symptoms.
**Objective:** The aim of this work is to provide an up-to-date overview of the treatment of psychotic symptoms in Parkinson's disease.
**Methods:** We describe 3 cases of development of psychotic symptoms, which occurred in patients with Parkinson's disease, and provide an update on the management of psychiatric symptoms manifestations in Parkinson's disease, by brief literature review.
**Results:** Case 1: 42-year-old man, married, received a diagnosis of PD at the age of 38, presented auditory hallucinations, which occurred 12 months following antiparkinsonian drugs use. Case 2: 58-year-old man, without any notable history, received a diagnosis of PD at the age of 41, presented jealousy delusions and behavioral disorders, which occurred 12 years following antiparkinsonian drugs use. Case 3: 76-year-old man, received a diagnosis of PD at the age of 40, presented visual hallucinations, subjective sensation of a presence and jealousy delusion, which occurred 26 years following antiparkinsonian drugs use.
**Conclusion:** Psychotic symptoms in Parkinson's disease are frequent. Management consists of treating psychotic symptoms without worsening motor symptoms related to hypo-dopaminergia.



## Introduction:-

Parkinson's disease (PD) is a chronic progressive neurodegenerative disease. Motor symptoms are the most common features (including extrapyramidal hypertension, stiffness, tremor and akinesia, hypokinesia, orthostatic hypotension, urinary incontinence) and may be accompanied by non-motor symptoms, including mood disturbance, cognitive impairment and psychotic symptoms. Non-motor, cognitive, or psychiatric symptoms have a significant impact on patients' functional autonomy and quality of life[1].

About 30% have hallucinations and about 5% have delusion. Persistent psychotic symptoms, especially delusions, are extremely distressing to patients and caregivers. Psychoticssymptoms are associatedwithpoorprognosis in PD [2,3]

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Treatment of PD psychosis is challenging: Dopaminergic therapies such as levodopa or dopamine agonists are commonly used to treat motor symptoms in PD, but can exacerbate psychosis. In contrast, typical antipsychotics prescribed for psychotic symptoms exacerbate motor symptoms due to dopaminergic antagonism, leading to severe morbidity. [4]

The aim of this work is to provide an up-to-date overview of the treatment of psychotic symptoms in Parkinson's disease. We report 3 cases of psychotic disorders in patients with Parkinson's disease who were followed indepartment of psychiatry of Mohammed V Military Teaching HospitalRabat in Morocco, and we performed a literature review on the treatment of Parkinson's disease psychosis.

**Clinical Presentation PD psychosis:**
We can summarize the clinical manifestations (Table 1): [5,6,7,8]:

**Table 1:-** Comparison of clinical manifestations between psychosis in the elderly and psychosis in Parkinson's disease.

| | Psychotic disorders in the elderly | PD psychosis |
|---|---|---|
| Perception disorders | • **Auditory, olfactory and visual hallucinations**<br>• **Intrapsychic hallucinations** | • **Minor hallucinatory phenomena: illusions, subjective sensation of a presence**<br>• **Visual hallucinations**<br>• **Lessfrequentauditory hallucinations** |
| Delusionthemes | • **Persecution, greatness, mystic, hypochondriac** | • **Persecution, infidelity, abandonment** |
| Emotionalexperience | • **Oftenpoor** | • **Anxiety with frequent marital conflict** |
| Judgement | • **Impaired judgment** | • **Less disrupted** |
| Insight | • **Negative** | • **Sometimespresent** |

There are no standardized diagnostic criteria for Parkinson’s disease psychosis. Some authors propose specific diagnostic criteria for the diagnosis. [9]

**Features:**
1. Occurs in patients with established diagnosis of Parkinson Disease
2. At least 1 symptom of: hallucinations, illusions, false sense of presence, delusions
3. Symptoms present for at least 1 month
4. May occur with or without: dementia, insight, medication for Parkinson disease

Differential diagnoses: Psychosic symptoms due to delirium, dementias, depression, schizophrenia, other psychiatric disorders

**Cases:**
**Case 1:**
42-year-old man, married, with a past medical history of consanguinity of first-degree relatives, received a diagnosis of PD at the age of 38, stabilized on Levodopa, Pramipexol and Amantadine. About 1 year after the beginning of the antiparkinsonian treatment, he presented psychotic symptoms such as auditory hallucinations and then a jealousy delusion. He was put on Quetiapine 150 mg per day, without improvement of the psychotic symptoms. Social functioning was impaired, which led to his divorce.

**Case 2:**
58-year-old man, without any notable past medical history, received a diagnosis of PD at the age of 41, progressively worsening under Levodopa, Amantadine and Pramipexol. He presented psychotic manifestations of

jealousy delusion and behavioral disorders 12 years after the beginning of his antiparkinsonian treatment. He was put on Quetiapine 200 mg daily. Without adequate control of psychotic symptoms.

**Case 3:**
76-year-old man, received a diagnosis of PD at the age of 40, with past medical a history of glaucoma, presented psychotic symptoms such as feeling of false presence, visual hallucinations, and delusions of jealousy about 26 years after starting PD medication with Bromocriptine and Piribedil, then Levodopa, Amantadine and Pramipexol. He was initially put on Clozapine 25 mg daily for management of psychotic symptoms, with improvement of psychotic manifestations, but the Clozapine was stopped because of neutropenia. He was then put on Risperidone 1 g daily, but due to the worsening of motor symptoms, he was put on Quetiapine 100 mg daily, then on Donepezil, but the psychotic symptoms persisted, until the patient's death.

## Discussion:-

The average age of diagnosis of PD is 58 years. 2/3 of the patients develop the disease between 50 and 70 years, 17% before 50 years and 15% after 70 years. The average duration of PD is 11 years [10].

In our study, all three cases had an age of onset of PD, before the age of 50 years. In case 1, the psychotic symptoms appeared 1 year after the start of antiparkinsonian treatment, in case 2, after 12 years, in case 3, after 26 years.

Management depends on the severity and impact of the psychotic symptoms. If psychotic symptoms are intermittent and non-disruptive, it is recommended that [6]:

1. Identification of medications that can potentially trigger psychotic symptoms.
2. Reducing the dose or stopping the medication
3. Monitoring for progressive worsening of psychotic behavior.

If the psychotic symptoms are not tolerated, with anxiety and behavioral problems:it is recommended to use a pharmacological approach[3,6,11,12,13].

As first-line therapy,Pimavanserinis recommended.Pimavanserin is a 5-HT2A receptor inverse agonist approved by the U.S. Food and Drug Administration (FDA) since 2016 for the treatment of patients with hallucinations and delusions associated with PD psychosis, available in the U.S. since 2016 The approved (FDA) recommended dose is 34 mg per day[3,6,11,12,13].

Pimavanserin is currently unavailable in Morocco.

As a second-line treatment, Clozapine, recommended by the American Academy of Neurology (AAN), has been shown to be effective and safe in placebo-controlled studies at mean doses of 25 to 36 mg per day. However, Clozapine is used to treat the psychotic symptoms of Parkinson's disease [3,6,11,12,13].

In the third line, Quetiapine was dosed at 50 to 150 mg per day, and although controlled studies showed no statistically significant difference compared to placebo, there was little effect on motor symptoms[3,6,11,12,13].

Quetiapine is used in clinical practice for the treatment of PD psychotic symptoms, but efficacy has not been consistently demonstrated in clinical trials [14].

Risperidone improves psychotic manifestations of Parkinson's disease and is not recommended due to frequent motor deterioration. Olanzapine and Aripiprazole are also not recommended by the European Federation of Neurological Societies (EFNS) and Movement Disorders Society-European Chapter (MDS-ES) and the American Academy of Neurology [3,6,11,12,13].

Cholinesterase inhibitors (donepezil, rivastigmine) are recommended in patients unresponsive or intolerant to atypical antipsychotics, regardless of the presence of dementia [3,6,11,12,13].

First-generation antipsychotics are not recommended because of the high risk of impairment and worsening of motor characteristics in PD. For example, haloperidol is associated with increased all-cause mortality in patients with Parkinson's disease [3,6,11,12,13].

In case 3,According to second-line recommendations,our patient was initially treated with Clozapine 25 mg daily and his psychotic manifestations improved, but clozapine was discontinued due to neutropenia.

In all 3 cases, our patients received quetiapinerespectively 150, 200, and 100 mg daily. But no significant improvement in psychotic manifestations was observed.

## Conclusion:-

Psychotic symptoms are frequent in Parkinson's disease. With a heavy and painful impact. Pimavanserin (not available in Morocco) is effective, recommended as first-line antipsychotic treatment. Clozapine is also recommended, but should be used with caution because of its hematological side effects. Quetiapine, Olanzapine and Aripriprazole should not be considered as first-line drugs: There are no statistically significant difference in placebo-controlled studies. In patients unresponsive or intolerant to atypical antipsychotics, a cholinesterase inhibitor may be warranted.

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