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IP International Journal of Comprehensive and Advanced Pharmacology

Journal homepage: www.ijcap.in

Short Communication

Pramipexole for symptoms of depression in patients with Parkinsonism/ Parkinson's disease

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Abstract

In patients with PD, depressive symptoms are seen in more than one-third of cases for which patients are prescribed conventional antidepressant drugs - NSRIs (noradrenaline serotonin reuptake inhibitors), SSRIs (selective serotonin reuptake inhibitors) and tricyclic antidepressants (TCAs). Pramipexole is a non-ergoline derivative dopamine agonist used for the treatment of Parkinsonism/Parkinson's disease (PD) as well as for treatment moderate to severe idiopathic Restless Legs Syndrome (RLS), has also been found useful and rather superior to some of these conventional anti-depressant drugs for improvement in the symptoms of depression in patients with PD. The available data from various studies suggests that pramipexole may be used as an alternative to conventional antidepressant drugs in patients with symptoms of depression in PD. This article highlights role of pramipexole in depression.

Keywords: Parkinson's disease/Parkinsonism, Pramipexole, Depression.

Received: 20-05-2025; **Accepted:** 25-06-2025; **Available Online**: 23-07-2025

1. Introduction

Almost one-third of the patients with Parkinsonism/Parkinson's disease (PD) have significant associated depressive symptoms, which further deteriorates the quality of life which is already affected. One of the recent meta-analysis review done to analyse the prevalence of major depressive disorder using data from 36 studies, it was observed that MDD is present in 17% of the individuals, 225 individuals had minor depression, 13% individual had dysthymia while clinically significant symptoms of depression were seen in 35% of individuals with parkinsonism.[1] A multicentric, multinational, observational study - PRODEST (PROfile of Depressive SympToms in Parkinson's disease), with more than 1000 patients enrolled in 24 centres in eight European countries observed a prevalence rate of major depressive disorder of 27.8% in individuals with PD.[2]

A number of antidepressant drugs including TCAs (tricyclic antidepressants), NSRIs (nor adrenaline serotonin reuptake inhibitors) and SSRIs (selective serotonin reuptake inhibitors) have been used to treat these depressive symptoms in Parkinsonism. This article discusses the role of Pramipexole dihydrochloride for depressive symptoms treatment in these patients and its use as an alternative to the conventional antidepressant drugs.

2. Pathophysiology of depression in Parkinsonism

Depressive symptoms in Parkinsonism result from a disturbance in the brain stem nuclei and cortical areas in the monoaminergic pathways.[3] Dopamine receptors of the D_3 subtype located in the limbic area are predominantly

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https://doi.org/10.18231/j.ijcaap.2025.018

responsible for regulating emotions and affective functions, and may thus be related to PD-associated depression.[4-6] In a study by Remy et al. where they used [^{11}C] RTI-32 which is an in vivo marker of nor adrenaline and dopamine transport, it was observed that depression in parkinsonism might was related to a loss of dopamine and nor adrenaline innervations in sub-cortical and cortical areas of the limbic system.[7] A number of other studies also show PD depressive symptoms to be related to catecholaminergic dysfunction.

A study by Ishibashi K et al. using ^{11}C-FLB 457 positron emission tomography (PET) scanning, demonstrates that pramipexole (at a dose of 0.25 mg) significantly binds to dopamine D_2/D_3 receptors present in the prefrontal cortex, amygdala, and medial and lateral thalamus, the regions known to have some relation to depression.[8] Most of the depressive symptoms in these patients are an expression of PD, rather than of a depressive syndrome. These areas may be the target sites of antidepressant action of pramipexole.[9]

3. Treatment of Depressive Symptoms in Parkinsonism Patients

The drugs commonly used for depressive symptoms in PD patients include tricyclic antidepressants (TCAs), nor adrenaline serotonin reuptake inhibitors (NSRIs) and selective serotonin reuptake inhibitors (SSRIs).[9]

A placebo-controlled, double-blind study done to compare the effect of TCA, SSRI's and placebo on depressive symptoms in PD patients showed that TCA - desipramine had better and faster control of depressive symptoms as compared to SSRIs and placebo.[9] Similarly, another placebo-controlled, double-blind study done to compare the effect of NSRI, SSRI and placebo on depressive symptoms in PD patients showed that nortriptyline was superior in controlling depressive symptoms as compared to SSRI - paroxetine and placebo. Thus the TCAs show better control of symptoms of depression and also reduction in motor symptoms in parkinsonism, but their use is limited due to higher incidences of side effects.[9]

4. Role of Pramipexole

Pramipexole dihydrochloride is a non-ergot dopamine agonist used for the treatment of idiopathic parkinsonism and for idiopathic Restless legs syndrome (RLS) with moderate to severe symptoms. In Idiopathic Parkinson's disease the dosage of Pramipexole used is 0.375 mg daily in three divided doses initially, followed by increase in dose by 0.125 mg every 5-7 days to 1.5-4.5 mg daily in three divided doses.

An open-label study was conducted to observe the effect of pramipexole on depression in 36 PD patients with normal or mild depression. Pramipexole was prescribed to these patents as either an add-on therapy to L-dopa or as monotherapy and the patients were re-evaluated after 3 months of pramipexole treatment. The evaluation was done by comparing the Unified Parkinson's Disease Rating Scale III (UPDRS), Hamilton Depression Rating Scale (HAM-D), Hoehn and Yahr scale (H&Y), and freezing of gait questionnaire before and after treatment, and the results showed significantly improved in these scores after treatment with pramipexole. Improvement in HAM-D score was also observed in non depressive PD patients.[10]

In another study involving 20 patients with PD, significant improvement was seen in depression after 2-3 months treatment with pramipexole, as shown by the decrease in the Zung self-rating depression scale (SDS) and the Unified Parkinson Disease Rating Scale (UPDRS) scores.[11]

Barone P et al conducted a 14-week multicenter, randomized trial to compare pramipexole with sertraline in depressed PD patients without motor complications, using the HAM-D scale. The study showed significantly higher improvement of depressive symptoms in pramipexole group and antidepressant effect of pramipexole in PD patients was not linked to improvement in motor symptoms.[12]

In a 12-week double-blind, multicenter, placebo-controlled clinical trial done using pramipexole in PD patients with stable motor function and on levodopa treatment, pramipexole group showed significant reduction in depressive symptoms as measured by Beck depression inventory score, compared to the placebo group.[13] No dose escalation of pramipexole was required to treat depressive symptoms in these studies.[10-12]

5. Conclusion

A large percentage of population with PD have significant depressive symptoms. In controlling these depressive symptoms in patients with PD, dopaminergic agonist pramipexole has been found to be significantly superior to placebo, and equal or better in efficacy when compared to the commonly used conventional drugs TCAs, NSRIs and SSRIs.

The data obtained from these studies suggest that pramipexole may be used as an alternative to conventional antidepressant drugs to treat depressive symptoms in PD patients, thus avoiding the risk of adverse events of antidepressants, besides having the added benefit of control of motor symptoms of Parkinson's disease.

6. Source of Funding

None.

7. Conflict of Interest

None.

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Cite this article: Singh A, Matreja PS, Singh H, Gupta AK, Kaur J. Pramipexole for symptoms of depression in patients with Parkinsonism/ Parkinson's disease. *IP Int J Compr Adv Pharmacol*. 2025;10(2):119–121.