Journal of Neuroimaging and Neuromedicine

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Management of Non-Motor Symptoms in Parkinson's Disease: A Practical Experience

Abstract

Introduction: Parkinson's disease (PD) is a neurodegenerative disorder with progressive motor and non-motor symptoms (NMS). Motor symptoms are more recognizable and easily assessed using a standardized scale for Movement Disorders. However, NMS has a significant role in affecting patients' quality of life, typically precedes motor symptoms, and can cause functional and cognitive deterioration in the long term. The neuropathological basis, classification, and management of NMS in PD are reviewed in this article, considering clinical experience, and using data from PD clinical trials.

Methodology: This article aims to revisit the diagnostic understanding, neuropathological mechanisms, symptoms' complex presentation, practical management options, and discussion of future emerging therapies.

Conclusion: The author has identified significant variability in the presentation of non-motor symptoms with Movement disorders and emphasizes the importance of a better understanding of neuropathological mechanisms, early detection, diagnosis, and implementation management to minimize disease burden and disabilities. The author has also identified emerging therapies requiring more focused research and trials before implementation.

Keywords: Parkinson's Disease, Non-motor Symptoms, Neuropathology, Management, Clinical Experience, Clinical Trials.

Review Article

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Received: 27 September, 2024; **Accepted:** 29 October, 2024; **Published:** 11 November, 2024.

Introduction

Although Parkinson's disease (PD) is still more often associated with the classic motor symptoms of tremor, rigidity, and bradykinesia, non-motor symptoms (NMS) also contribute to the disability and distress that patients experience. NMS include cognitive impairment, mood disorders, autonomic dysfunction, musculoskeletal and neuropathic pain, neurogenic bladder and constipation, visual disturbances, balance impairments, sexual dysfunction, exocrine deficiency and sleep disturbances. Therefore, they should be considered in assessing and treating the disease since they often occur early, can be severe, and contribute significantly to the burden of PD [1]. In a multidisciplinary practice, where all input is considered necessary, NMS is now the focus of clinical trials and practical clinical experience in managing PD. This article reviews the medical evidence for the management of NMS in PD.

Neuropathological Basis

The Braak theory posits that non-dopaminergic pathways play a significant role in developing NMS in PD. The loss of non-catecholaminergic neurons in the dorsal motor nucleus of the vagus and surrounding area is quite advanced by the time loss of nigrostriatal dopaminergic neurons in the

substantia nigra is well underway, leading to the delays in motor changes that often accompany PD. The early non-dopaminergic involvement of PD pathophysiology adds another complexity and a challenge to adequately managing and treating the disease.

Classification of PD Based on NMS

PD can be classified into three phases based on the presence and progression of NMS:

1. Pre-clinical phase: Characterized by positive biological markers without clinical symptoms.
2. Pre-motor phase: Presence of NMS without motor symptoms.
3. Motor phase: Co-existence of motor symptoms and NMS.

Common Non-Motor Symptoms and Their Management

1. **Drooling:** This is primarily due to impaired mouth movements and swallowing. Management includes chewing gum, anticholinergics, and botulinum toxin injections. Clinical trials have shown that botulinum toxin injections effectively reduce drooling in PD patients [2].
2. **Anosmia:** Olfactory dysfunction affects up to 90% of patients. Management involves compensatory measures such as smoke detectors. Olfactory dysfunction is a well-documented early symptom of PD [3].
3. **Dysphagia:** Swallowing difficulties managed with speech therapy and oro-motor exercises. Speech therapy has been shown to improve swallowing function in PD patients [4].
4. **Nausea and vomiting:** Managed with domperidone and dietary adjustments. Domperidone is commonly used to manage gastrointestinal symptoms in PD [5].
5. **Constipation:** This can be managed with hydration, dietary fibre, exercise, and pharmacological agents like laxatives and cholinomimetics. Clinical trials support the use of these interventions in PD [6].
6. **Bladder dysfunction:** This can be managed with lifestyle changes and medications like anticholinergics and botulinum toxin injections. Bladder dysfunction is common in PD and can be managed with these interventions [7].
7. **Pain:** This is managed by addressing primary and secondary causes, including muscle rigidity and dyskinetic movements. Pain management in PD is crucial and involves multiple strategies [8].
8. **Cognitive dysfunction and dementia:** These can be managed with cognitive activities, exercise, a healthy diet, and cholinesterase inhibitors. Cognitive decline is a significant concern in PD, and these interventions are supported by evidence [9].
9. **Mood disorders:** Depression and anxiety are common, managed with pharmacological and non-pharmacological approaches. Mood disorders are prevalent in PD and require comprehensive management [10].
10. **Sexual dysfunction:** Managed by addressing autonomic degeneration and related factors. Sexual dysfunction is a significant issue in PD, and various treatments are available [11].
11. **Orthostatic hypotension:** This is managed with hydration, salt intake, and medications like domperidone and midodrine. Orthostatic hypotension is a common autonomic symptom in PD [12].
12. **Sleep disorders:** Managed with medications like SNRI, methylphenidate, and modafinil. Sleep disorders are prevalent in PD and require targeted interventions [13].

Discussion

The management of NMS in PD requires a multifaceted approach, addressing each symptom with tailored interventions. Early identification and treatment of NMS can significantly improve the overall well-being of PD patients. This article highlights the importance of a comprehensive management plan that includes pharmacological and

non-pharmacological strategies. The author recommends reviewing existing model of care and consider a novel approach to starting an integrated movement assessment program targeting assessment for non-motor symptoms and implement a multidisciplinary assessment and recommendations to bridge the gap between primary care physicians and Neurologist. (Integrated Movement assessment program – Illawarra and Shoalhaven local health district).

Emerging Therapies

Emerging non-motor symptoms (NMS) in Parkinson's disease (PD) are an exciting area of research aiming to improve the quality of life for patients. Here are some of the promising developments:

Gene Therapy: "These therapies aim to enhance the function of glucocerebrosidase, an enzyme that helps in the degradation of cellular waste [1].

Neuroprotective Agents

GLP-1 Agonists: "Drugs like exenatide, initially used for diabetes, are being evaluated for their neuroprotective effects in PD [14]."

Nilotinib: "A cancer drug that has shown promise in reducing neurodegeneration and improving cognitive function in PD patients [15].

Targeted Drug Delivery

Innovative drug delivery systems are being developed to target specific brain regions affected by PD. These include:

Intranasal delivery: "This method bypasses the blood-brain barrier, allowing direct delivery of therapeutic agents to the brain [16].

Nanoparticles: "These are being used to deliver drugs more effectively to the brain, potentially improving the management of NMS [17].

Cell-Based Therapies

These therapies address motor and non-motor symptoms by regenerating healthy neural tissue [18].

Non-Pharmacological Interventions

Non-pharmacological approaches are gaining attention for their potential to manage NMS in PD. These include:

Cognitive behavioural therapy (CBT): "Effective in managing depression and anxiety in PD patients [19].

Photo biomodulation: "Used to treat sleep disorders and depression by regulating circadian rhythms [20].

Exercise and physical therapy: "Regular physical activity has been shown to improve cognitive function, mood, and overall quality of life in PD patients [21].

Novel Pharmacological Treatments

Several new drugs are in the pipeline, targeting various NMS:

Pimavanserin: "Approved for treating psychosis in PD, it is also being studied for its effects on depression and sleep disorders [22].

Opicapone: "A COMT inhibitor that helps manage motor fluctuations, potentially improving overall well-being [23].

Magnetic Field Therapy

Transcranial magnetic stimulation (TMS) and other forms of magnetic field therapy are being investigated for their potential to alleviate depression, cognitive impairment, and other NMS in PD [24].

Conclusion

Non-motor symptoms in Parkinson's disease are diverse and significantly impact patients' quality of life. Effective management requires a thorough understanding of the neuropathological basis and a tailored approach to each symptom. By focusing on NMS, healthcare providers can offer more holistic care to PD patients, improving their overall quality of life.

While these emerging therapies offer hope for better management of non-motor symptoms in Parkinson's disease, it is crucial to consider their safety profiles and potential side effects.

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Citation: Bala Vaidya. “Management of Non-Motor Symptoms in Parkinson’s Disease: A Practical Experience.” J Neur Imag Neur Med (2024): 109. DOI: 10.59462/JNINM.2.1.109