Cardiovascular Autonomic Dysfunction in Idiopathic Parkinson's Disease

Cardiovascular dysautonomia is an integral part of Parkinson's disease (PD) and includes orthostatic hypotension, supine hypertension, nocturnal hypertension, labile blood pressure, and absence of decrease in blood pressure during night (non-dipping) and heart rate variability.[1] These can occur as an adverse effect of dopaminergic treatment as well as independent of drug effect. Cardiovascular autonomic dysfunction is not limited to advanced stages of PD and can occur even in the early mild stage of the disease.[2] Orthostatic hypotension affects 20–40% of PD patients. Cardiovascular autonomic dysfunction is associated with an increased risk of cognitive impairment, white matter hyperintensities, fatigue, falls, and mortality in patients with PD.[3,4]

The pathophysiology involves the degeneration of both the peripheral autonomic nervous system as well as the involvement of central neural networks.[5] Lewy bodies have been demonstrated not only in central autonomic pathways but also in sympathetic ganglia and sacral plexus. Moreover, genetic factors also play a key role as cardiac sympathetic denervation has been observed in synuclein-alpha (SNCA) duplications and triplications and glucocerebrosidase (GBA) mutations.[6]

Various assessment tools are available to assess cardiovascular dysautonomia such as Scale for outcomes in Parkinson's disease for autonomic symptoms (SCOPA-AUT), composite autonomic symptom scale, orthostatic grading scale, and novel non-motor symptoms scale.[7]

The results of the study from Christian Medical College and Hospital, Ludhiana published with this commentary are consistent with the literature review.[8] Cardiovascular autonomic dysfunction was observed in two-thirds of the patients with impairment of both sympathetic and parasympathetic autonomic nervous systems. The authors highlighted the occurrence of dysautonomia even in the early stages of the disease and progressive worsening with age and disease severity. They also stressed the importance of blood pressure variability and abnormal dipping patterns on ambulatory blood pressure monitoring as a potential marker of dysautonomia. However, the authors have not studied the natural history of autonomic dysfunction in PD. Merola *et al.*[9] in their prospective cohort study of 131 PD patients found progression in the severity of orthostatic hypotension by 20% over 1 year with greater deterioration in activities of daily living and health care utilization.

Cardiac imaging using iodine-123-metaiodobenzylguanidine (^{123}I-MIBG) used to quantify postganglionic cardiac sympathetic innervation has a sensitivity and specificity of 90 and 83%, respectively, in differentiating PD from atypical parkinsonism.[10] Reduced cardiac ^{123}I-MIBG uptake is associated with PD and is preserved in multiple system atrophy. However, 50% of de novo early-stage PD may show preserved cardiac sympathetic innervation and up to one-third of patients with multiple system atrophy have reduced cardiac tracer uptake.[11,12]

Treatment of neurogenic orthostatic hypotension includes correction of aggravating factors, non-pharmacological measures, and drug therapies. Fludrocortisone expands intravascular volume and midodrine and droxidopa increase blood pressure by increasing peripheral vascular resistance.[13]

The effects of deep brain stimulation on cardiovascular autonomic dysfunction are controversial and undetermined at present with some studies showing benefits while others have demonstrated no modification or even adverse outcomes.[14]

Novel neuroimaging techniques have highlighted the role of the medulla oblongata and the involvement of thalamo-striatal-hypothalamic connections as demonstrated with the help of diffusion tensor imaging and functional Magnetic resonance imaging (MRI) studies.[15,16]

To conclude, cardiovascular autonomic dysfunction is an important non-motor symptom of PD that can occur across all the stages of the disease. The affection of both central and peripheral autonomic structures is responsible. Understanding its pathophysiological basis as well as the role of functional connectivity of brain regions involved in the complex process of autonomic integration will pave the way for the development of novel therapeutic approaches in the management of this disabling symptom.

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