Parkinson disease (PD) is classified as a disease of abnormal motor function and is associated with decreased levels of dopamine in the brain. Parkinson disease also entails nonmotor symptoms that are not normally discussed. Nonmotor symptoms include sleep dysfunction, sensory symptoms, autonomic dysfunction, mood disorders, and cognitive abnormalities. This issue of CLIPS briefly summarizes an article that reviews the treatment of nonmotor symptoms in patients with PD and the recommendations that can be made from the review of current literature. If you need further information, please contact the Samford University Drug Information Service at (205) 726-2659.


**Description of the Analytic Process**

- Therapies reviewed consisted of pharmaceuticals, continuous positive airway pressure machine in patients with sleep abnormalities, dietary modifications, homeopathic treatments, surgery, and interventional therapies such as electroconvulsive therapy.
- Articles were excluded if they did not include PD or treatment of nonmotor symptoms of PD or if they related to the treatment of cognitive or mood disorders in PD or the treatment of sialorrhea with botulinum toxin.
- Levels of recommendations are as follows
  - **A** = Established as effective, ineffective or harmful (or established as useful/predictive or not useful/predictive) for the given condition in the specified population. (Level A rating requires at least two consistent Class I studies.)
  - **B** = Probably effective, ineffective or harmful (or probably useful/predictive or not useful/predictive) for the given condition in the specified population. (Level B rating requires at least one Class I study or two consistent Class II studies.)
  - **C** = Possibly effective, ineffective or harmful (or possibly useful/predictive or not useful/predictive) for the given condition in the specified population. (Level C rating requires at least one Class II study or two consistent Class III studies.)
  - **U** = Data inadequate or conflicting; given current knowledge, treatment (test, predictor) is unproven.

**Sexual Dysfunction**

- Sildenafil citrate enabled men to achieve and maintain an erection allowing for an improved sex life compared to placebo as well as significantly higher self ratings (3.71 vs 1.56 respectively) for obtaining an erection.

- Sildenafil citrate 50 mg is possibly effective in the treatment of erectile dysfunction in PD (Level C).

**Orthostatic Hypotension**

- Small studies have been conducted to evaluate orthostatic hypotension (OH) in PD patients, but evidence and support for specific agents is lacking.
- At this time the data is insufficient to support or deny the treatment of OH in PD patients (Level U).

**Urinary Incontinence**

- Apomorphine, a dopamine agonist, resulted in improved voiding efficiency and increased flow rates upon urination in one small study.
- Beneficial improvements in bladder capacity and volume after deep brain stimulation of the subthalamic nucleus have been demonstrated in two small studies.

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Urinary Incontinence (continued)

- The data to support or reject the use of apomorphine or deep brain stimulation to treat urinary incontinence in PD is lacking at this time (Level U).

Gastrointestinal Symptoms

- Constipation is a common result of autonomic dysfunction in PD patients.
- Polyethylene may improve bowel movement frequency and stool consistency.
- Botulinum toxin may reduce anal tone during straining.
- Polyethylene glycol may improve constipation symptoms in PD, but evidence is inconclusive regarding botulinum toxin (Level U).

Excessive Daytime Somnolence (EDS)

- Modafinil, an FDA-approved medication for the treatment of narcolepsy, improved patient perception of wakefulness, but may not improve maintenance of wakefulness (Level A)

Periodic Limb Movements (PLMS)

- Cabergoline was found to increase the number of awakenings and stage shifts, but reduced PLMS during sleep.
- Carbidopa/levodopa reduced the occurrence of spontaneous movements in bed from 48/night to 28-33/night.
- Carbidopa/levodopa most likely reduces PLMS and should be considered (Level B), but data is lacking on the use of non-ergot dopamine agonists (Level U).

REM Sleep Behavior Disorder (RBD)

- RBD is a form of parasomnia and is characterized by patients acting out violent dreams during the REM sleep stage
- Data is insufficient to recommend or deny treatment of RBD in PD (Level U)

Fatigue

- Methylphenidate has shown improvements in fatigue symptoms over placebo and may be useful in the reduction of fatigue and fatigue symptom in PD patients (Level C)

Anxiety

- Levodopa controlled release and immediate release formulations show a trend toward reduction in anxiety in PD patients, however the results were statistically insignificant.
- Data at this time is insufficient to promote or deny the treatment of anxiety with levodopa in PD patients (Level U).

Recommendations for Future Research

- Trials regarding drugs in the treatment of nonmotor symptoms in PD are lacking and are urgently needed.
- Symptoms which would benefit from further research include sleep disorder, autonomic symptoms, psychological symptoms, sensory dysfunction, and other nonmotor symptoms including weight loss, anorexia and leg edema.