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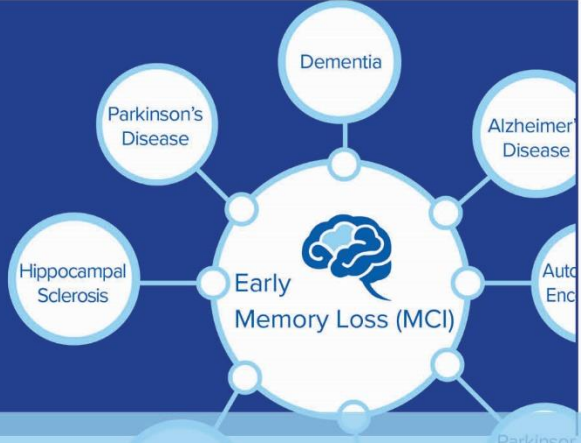

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Non-Motor Symptoms in Parkinson's Disease – Part Two – Dr. Sheila Baez-Torres

In our previous newsletter we discussed the non-motor symptoms commonly seen in PD. While motor symptoms are known to be caused by loss of dopaminergic cells in the brain, the non-motor symptoms (NMS) are the result of changes in non-dopaminergic cells. Dr. K. Seppi et al, published an evidence-based review of the current treatments for NMS of PD[1]. Thirty- seven studies were reviewed to identify "clinically useful", "possibly useful", and "not useful" options. In this article we are going to briefly summarize the "clinically useful" and "possibly useful" interventions for some NMS.

DEPRESSION – Commonly seen in patients with PD. While it is difficult to differentiate as premorbid or comorbid, treatment may help quality of life and they may become more engaged in their healthcare. Pramipexole is a dopamine agonist determined to be "clinically useful" for treating depression. Venlafaxine (a SNRI) was determined "clinically useful", and several SSRIs (citalopram, sertraline, paroxetine and fluoxetine) were thought to be "possibly useful" in treating depression. While nortriptyline, amitriptyline, and desipramine are "clinically useful" TCAs, caution is recommended in elderly patients with PD, given negative cognitive side effects.

DEMENTIA - Rivastigmine (AChEI) was found to be "clinically useful". Donepezil and galantamine (AChEI) are considered "possibly useful". In the case of nondementia cognitive impairment, there is insufficient evidence to conclude any of the AChEIs are efficient, but with any of the three, rivastigmine seems to have some benefit[2].

PSYCHOSIS – A common challenge in PD. It is not only disruptive to patients and families but is also a major limiting factor when trying to optimize the treatment of motor symptoms by using dopaminergic drugs. Pimavanserin is considered "clinically useful" and efficacious treatment for PD psychosis. Clozapine is also "clinically useful", but its risks (severe neutropenia-requiring weekly blood count, risk of orthostatic changes, bradycardia, seizures, myocarditis and cardiomyopathy) make this drug very challenging to use. A third and commonly used option is quetiapine, which is considered "possibly useful" to control psychosis.

INSOMNIA – Melatonin, eszopiclone, and rotigotine are all considered "possible useful". Modafinil and CPAP may be "possibly useful" in the treatment of excessive daytime sleepiness and sudden onset of sleep. Nonpharmacological interventions like CPAP may be useful but perhaps difficult to tolerate by many patients.

AUTONOMIC DYSFUNCTION – Includes orthostatic hypotension (OH), sexual dysfunction, constipation, anorexia, nausea, excessive drooling, and urinary frequency, urgency and incontinence. Fludrocortisone, midodrine, and droxidopa are all considered "possibly useful". Sildenafil was found efficacious and clinically useful alternative for sexual dysfunction. Probiotics, and prebiotic fiber are "clinically useful" in the treatment of constipation. Lubiprostone and macrogol were found both "possibly useful", with acceptable risks without specialized monitoring needed. Domperidone is likely efficacious and considered "possibly useful" to control the anorexia, nausea, and vomiting associated with dopaminergic agents. Among all the drugs available for the treatment of urinary dysfunction, solifenacin was found "possibly useful" for the treatment of overactive bladder in patients with PD.

SIALORRHEA – Until recent years, drooling was not addressed as a complication of PD, and although a common and embarrassing problem, it was dismissed and undertreated. Chemodenervation with botulinum toxin type A and B is "clinically useful" controlling sialorrhea with minimal side effects and is well tolerated. The Compass Clinic treats sialorrhea with chemodenervation.

FATIGUE – One of the most difficult to treat NMS. Only two studies were reviewed by Seppi et al in which fatigue was part of the inclusion criteria. Among them, rasagiline was found "possibly useful" improving fatigue.

Many drugs such as safinamide, memantine, rotigotine, caffeine, domperidone, ipratropium, and methylphenidate were excluded but are under investigation or anecdotal use review for treatment of NMS of PD. It is important to remember while we are treating symptoms, we must treat with the lowest effective dose for each patient.

Similarly, we cannot underestimate the benefits of exercise, acupuncture, massage, cognitive behavioral therapy, physical and occupational therapy, transcranial direct current stimulation, meditation and other therapies. A multidisciplinary approach is needed for managing Parkinson's Disease.

[1]K. Seppi, MD K. R. Chaudhuri, MD et at. Update on Treatments for Non-Motor Symptoms of PD- An Evidence-Based Medicine Review. Movement Disorders, Vol 34, No 2, 2019

[2]Mamikonvan E, Xie SX, et at. Rivastigmine for mild cognitive impairment in PD: A placebo-controlled study. Mov Disord 2015; 30:912-918

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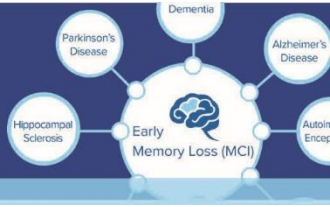

COMMUNITY RESOURCES

Lewy Body Support Group
2nd Monday of the Month at 4:30pm-6:30pm
Synexus Conference Room, 5th Floor
100 W Gore St, 5th Floor, Orlando, Fl 32806
Contact for More Info: Sue Bouder 914-589-2004

Lewy Body Dementia Association – www.LBDA.org
National Parkinson's Foundation – www.Parkinson.org
Parkinson's Association of Central Florida – www.ParkinsonCF.org
Michael J Fox Foundation – www.MichaelJFox.org
Brain Fitness Club- www.BrainFitnessClub.net
BrainFlex Wellness Club – www.brainflexwellness.com
Alzheimer's & Dementia Resource Center, www.adrccares.org , 407-436-7750
Alzheimer's Association - www.alz.org
Alzheimer's Disease and Related Dementias (ADEAR)/ NIA www.nia.nih.gov/health/alzheimers

New

Dementia Friendly Dining at The Meatball Stoppe
7325 Lake Underhill Rd. Orlando, FL 32822
Contact Toni Gitles for more information,
407-304-6534 or Tonigitles@gmail.com

SYNEXUS

Current Trial Count

Alzheimer's Disease
Disease modifying, symptomatic & agitation trials: 6
Parkinson's Disease
Disease modifying & symptomatic trials: 2
Dementia with Lewy Bodies
Symptomatic trial: 1
ALS:1

A Message From Dr. Goodman

Very encouraging news was released in October 2019 concerning Alzheimer's Disease treatment. Aducanumab, an antibody developed to reduce the amount of amyloid, one of the two signature AD proteins, has been in development for several years with initial discouraging results. In fact, the two phase 3 trials, EMERGE (1,638 patients) and ENGAGE (1,647 patients), were stopped in Spring 2019 due to discouraging early futility analysis. However, further analysis of a larger data set, including a longer-term analysis with the higher dose, demonstrated clear cut efficacy, both in removal of the signature protein from the brain as well as clinical benefit. Not only was the targeted amyloid protein reduced, the other signature protein tau, which correlates with clinical impairment/ neurodegeneration, was also found to be lowered in the spinal fluid of these patients. Clinically speaking, there was a 40% change in ADLs in patients receiving the antibody. These positive results triggered the FDA to give permission to the pharmaceutical companies (Biogen/ Eisai) to file for approval and a "Biologics License Application" (BLA) will be filed this year. If approved, this will be the first disease modifying treatment approved for patients with Alzheimer's Disease and represents a potential game changer in our treatment. These results renew life in the "amyloid hypothesis" as playing a role in the pathogenesis in Alzheimer's Disease and will lead only to further efforts to successfully target this protein. Stay tuned for more information.

If approved however, it is estimated that treatment could cost up to $5,000 per month per patient. With the growth of Alzheimer's disease in the aging population, treatment may be difficult to access. We as healthcare providers need to try and make sure our patients can obtain access to treatment. It is still of upmost importance to evaluate those with cognitive complaints for the possibility of early Alzheimer's Disease to make healthier lifestyle choices and to explore screening for a clinical trial if appropriate.

Synexus (formerly Bioclinica) was a site for these two trials. The patients that participated in these trials will have the opportunity to resume treatment as part of the trial to gather even more data.