Effect of Probiotics Supplementation in the Treatment of Parkinson's Disease

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Abstract

Parkinson's Disease (PD) is a neurodegenerative disease that results from the depletion of dopamine-secreting nerve cells. The mainstay of treatment for PD is Levodopa, a precursor to dopamine, which helps replenish dopamine levels in the body. However, this treatment is not curative and does not delay disease progression. PD, as an alpha-synucleinopathy, is hypothesized to have a potential pathway of disease development and progression through the brain-gut axis. This literature review investigated the effect of probiotics supplementation in the treatment of PD. Although the analysis of six articles demonstrated only one study with definitive benefits of probiotics supplementation in PD, it was concluded that probiotic supplementation should be considered an adjunct therapy in PD treatment due to its generally safe profile.

Introduction

Every year, approximately 50,000 people are diagnosed with PD, resulting in 500,000 people living with the disease at any given time in the U.S. PD is a neurodegenerative disease resulting from the loss of nerve cells that secrete dopamine, an important neurotransmitter that plays an essential role in rewards and behavior, pleasure, and motor function. Without this essential neurotransmitter, medical conditions such as PD can develop, affecting motor function. Current available treatment focuses on compensating for dopamine deficiency, primarily Levodopa, a precursor to dopamine. However, such treatment only provides symptomatic relief without hopes for a cure or even a delay in its degeneration. Over the past decade, there have been increasing studies exploring a potential connection between PD and gut microbiome. PD is one of the alpha-synucleinopathies, a group of neurodegenerative disorders associated with an accumulation of pathologic α-synuclein protein along the brain-gut axis. The theory that pathologic α-synuclein originates and ascends from the gut into the brain stems from the presence of common GI symptoms (abnormal salivation, defecatory dysfunction, dysphagia, constipation, and nausea) preceding the classical PD motor symptoms. Although the mechanism behind the theory is still widely unknown, it is suspected that the propagation of pathologic α-synuclein from the gut to the brain occurs via the vagal pathway.

Methods

A literature search was conducted on Google Scholar and PubMed in November 2019. Through the search, ten articles were identified with the highest relevance to the topic. The list was further narrowed down to six articles and analyzed, identifying those with the highest level of evidence with clinical relevance to the topic.

Results

The six studies analyzed included one randomized control trial (RCT) study, one cohort study, and four case control studies. An analysis of gut microbiota composition and UPDRS (Unified Parkinson's Disease Rating Scale) scores were used as outcome measurements in most of the studies. Some studies also included other outcome parameters such as short chain fatty acids (SCFA) and metabolic protein levels.

Table 1. Comparison of Study Designs

Study	Design	Total N	Population Demographics	Control	Study/Intervention Group	Outcome measurements
Bedarf et al. (2017)	Case Control	59	31 PD patients & 28 matched healthy individuals	Healthy individuals	Early-stage Levodopa-naïve PD patients	Gut microbiota composition; UPDRS
Hill-Burns et al. (2017)	Case Control	348	212 PD patients & 136 healthy individuals	Healthy individuals	PD patients	Gut microbiota composition; UPDRS; HY; SCFA
Minato et al. (2017)	Cohort	36	PD patients (2 year follow up)	Stable group	Deteriorated group (high UPDRS)	UPDRS; MOCA-J; HY; LBP; gut microbiota composition
Scheperjans et al. (2015)	Case Control	144	72 PD patients & 72 matched healthy individuals	Healthy individuals	PD patients	Gut microbiota composition, UPDRS
Tamtaji et al. (2018)	RCT	60	50-90 y/o PD patients	Placebo x12 weeks	Probiotic supplement[1] x12 weeks	MDS-UPDRS; metabolic protein levels (CRP, MDA, GSH, insulin)
Unger et al. (2016)	Case Control	68	34 PD patients & 34 healthy age-matched individuals	Healthy age-matched individuals	PD patients	Gut microbiota composition, SCFA

Key: UPDRS = Unified Parkinson's Disease Rating Scale; MOCA-J = Montreal Cognitive Assessment (Japanese version); HY = Hoehn and Yahr scale; LBP = lipopolysaccharide-binding protein; RCT = Randomized Control Trial; MDS-UPDRS = Movement Disorders Society-Unified Parkinson's Disease Rating Scale; CRP = C-reactive protein; MDA = malondialdehyde; GSH = glutathione; SCFA = short chain fatty acids

[1] Supplement contains *Lactobacillus acidophilus, Bifidobacterium bifidum, Lactobacillus reuteri, and Lactobacillus fermentum.*

Table 2. Comparison of Results/Measurement Parameters

Study	Change in gut microbiota composition	[MDS]-UPDRS	SCFA	CRP	MDA	GSH	Insulin	LBP
Bedarf et al. (2017)	S	NS	NA	NA	NA	NA	NA	NA
Hill-Burns et al. (2017)	S	NS	S	NA	NA	NA	NA	NA
Minato et al. (2017)	S	S	NA	NA	NA	NA	NA	NS
Scheperjans et al. (2015)	S	NS	NA	NA	NA	NA	NA	NA
Tamtaji et al. (2018)	NA	S	NA	S	S	S	S	NA
Unger et al. (2016)	S	NA	S	NA	NA	NA	NA	NA

Key: S = significant; NS = not significant; NA = not available/measured

Change in gut microbiota composition
S = significant difference of gut micro in study vs control group
NS = no significant difference

UPDRS
S = difference in UPDRS (P<0.05)
NS = no significant change in UPDRS

SCFA
S = reduced in PD pts
NS = no reduction in PD

CRP
S = reduced CRP (P<0.05) w/ probiotics
NS = no reduction in CRP

MDA
S = reduced MDA (P<0.05) w/ probiotics
NS = no reduction in MDA levels

GSH
S = increased GSH (P<0.05) w/ probiotics
NS = no reduction in GSH levels

Insulin
S = reduced insulin (P<0.05) w/ probiotics
NS = no reduction in insulin levels

LBP
S = reduced LBP (P<0.05) in deteriorated group
NS = no reduction in LBP

Discussion

While only one article had directly assessed the effect of probiotic supplements on PD patients and concluded that probiotics had favorable effects on multiple parameters of PD (including significantly decreased UPDRS scores, reduced sensitivity to CRP (C-reactive protein), and reduced insulin levels and resistance with a rise in insulin sensitivity), other studies provided supporting evidence of an association between certain microbial groups and severity of PD symptoms. Notably, a statistically significant reduction in *Prevotellaceae, Bacteroidetes, Bacteroides, Erysipelotrichaceae, Clostridium leptium*, *Faecalibacterium, Lactobacillaceae*, and *Enterococcaceae* were identified in PD patients when compared to their control group counterparts. In contrast, there was an increase in *Verrucomicrobiaceae, Firmicutes, Ruminococcaceae,* and *Enterobacteriaceae* in PD microbiome. In one study, *Enterobacteriaceae* was noted to have a positive correlation with the severity of postural instability and gait difficulty in PD while another study associated diminishing *Bacteroides fragilis* levels with worsening UPDRS scores.

Conclusion

Probiotic supplementation should be considered as an adjunct therapy to PD treatment regimen. Since probiotics have a generally safe profile, the benefits likely outweigh the risks in these cases. Future research can further explore large-scale clinical trials of probiotics use in PD patients. Long-term studies can also be considered to study the effect of probiotics on disease progression over time.

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