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The Effect of Broad-Spectrum Dietary Supplementation on Quality of Life, Symptom Severity, and Functioning in Multiple Sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a progressive neurodegenerative disease that exerts a significant quality-of-life toll on patients. According to the literature, broad-spectrum dietary supplementation including a variety of nutrients, polysaccharides, and compounds may improve the quality of life, functionality, and symptom severity in people with MS. Individuals ($n = 15$) diagnosed with relapsing-remitting MS (RRMS) for an average of 12.4 years (SD = 7.4; R = 2, 25) were enrolled in a one-year open-label clinical trial in which they consumed a broad-spectrum dietary supplement regimen three times daily. Participants were assessed at baseline and at 3, 6, 9, and 12 months with the following: (1) Functional Assessment of MS (FAMS), (2) the EQ-5D-3L, (3) Beck Depression Inventory-II (BDI), (4) Health Conditions Discomfort Scale (HCDS), and (5) Self-Assessment of Severity of MS Symptoms Scale (SASMSSS). Participants included seven females and eight males (M age = 51.3 years; SD = 7.2; R = 38, 65). Few minor gastrointestinal effects were reported. At the end of the intervention, participants showed significant improvements in all outcome measures, particularly functionality on the FAMS, overall quality of life on the EQ-5D-3L, fewer depressive symptoms on the BDI, and improved severity of symptoms on the HCDS and the SASMSSS. Our results suggest that dietary supplementation containing a variety of nutrients can improve the quality of life, severity of disease symptoms, and functionality in MS patients. These findings are clinically promising for MS patients, given the lack of treatment options geared toward improving quality of life in this population.

KEYWORDS

dietary supplement; multiple sclerosis; polysaccharide; quality of life; symptom severity

Introduction

Multiple sclerosis (MS) affects approximately 2.5 million people worldwide (Asche et al. 2010; Campbell et al. 2014; Livingston et al. 2016), and according to the latest *Atlas of MS* and other epidemiological work, the incidence of the disease is increasing (Trojano

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et al. 2012; Browne et al. 2014). MS sufferers live with significant disability and decreased functional capacity, and are often dependent on others for their activities of daily living (Ford et al. 2001). As a result, MS has catastrophic consequences for both patients and caregivers, thereby making the study of effective and safe treatment options an important endeavor.

No cure for MS currently exists, and a major treatment challenge for MS is the risk-benefit profile of the FDA-approved MS drugs, as most of them are associated with severe adverse and life-threatening side effects, including progressive multifocal leukoencephalopathy, which is irreversible and potentially fatal (Killestein et al. 2014; Rosenkranz et al. 2015; Lehmann-Horn et al. 2016; Schwab et al. 2017; Vargas and Tyor 2017). Unfortunately, these very frequent side effects lead to decreased quality of life for MS patients.

The high symptom burden experienced by MS patients and the frequent treatment side effects have led to greater interest in dietary supplement options. Poor nutrition has been demonstrated to impair neurological performance and health outcomes (Balto et al. 2017). In addition, diets high in saturated fats and low in both polyunsaturated fatty acids (PUFA) and antioxidants appear to play a role in MS incidence (Jahromi et al. 2012; Adamo 2014; Bagheri et al. 2014; Loken-Amsrud et al. 2015). Omega-3/6 fatty acids, antioxidants, and vitamin D have been coupled with dietary modifications to treat or prevent MS or to address disease-associated symptoms (Bagheri et al. 2014). Relapse severity and duration decreased among participants taking a PUFA supplement compared to a placebo (Dworkin et al. 1984). Quality of life, fatigue, and the relapse rate moderately improved in relapsing-remitting (RR)MS patients eating a low-fat diet supplemented with omega-3 PUFA for one year (Weinstock-Guttman et al. 2005). However, vitamin D and PUFA supplementation have also shown no benefit on clinical measures of MS in other studies (Kampman et al. 2012; Torkildsen et al. 2012).

Moreover, the science of glycomics (i.e., the investigation of the structure and biosynthesis of organic saccharides; Varki et al. 2015) may provide new physiologic treatment targets for MS. Our group has used various polysaccharide formulas combined with other nutrients to show significant quality of life improvements in both healthy adults and those with chronic diseases. We showed statistically and clinically significant improvement in cognitive functioning in persons with moderate to severe Alzheimer's disease after 12 months of a dietary supplement containing polysaccharides, antioxidants, and PUFAs (Lewis et al. 2012). We also demonstrated improvement in other quality of life indicators and depressive symptoms in response to magnesium sulfate, vitamin B complex, and a broad-spectrum multinutrient formula (Lewis, Cutrono, et al. 2014; Lewis, Melillo, et al. 2014; Mehdi et al. 2017).

While isolated nutrients have shown modest benefit in overall quality of life, we hypothesize that broad-spectrum dietary supplementation, including polysaccharides and other bioactive compounds, may potentially lead to better improvements for MS patients. Given the rising incidence, cost, and symptom severity of MS, along with the absence of curative treatment, the examination of a broad-spectrum dietary supplement regimen is justified. Thus, the purpose of the study is to investigate the effect of a 12-month course of a broad-spectrum dietary supplement regimen on quality of life, symptom of disease severity, and functionality in a sample of MS patients.

Methods

Study participants

Participants ($n = 15$) with RRMS were recruited from consecutive referrals to the Joanne P. LaGanke MS Center in the North Central Neurology Associates outpatient facility (Cullman, AL) from 2007 to 2008. The study was conducted with the approval of the DFW Micronutrient Counsel Institutional Review Board for human subject research, which operates within the standards set forth by the Helsinki Declaration of 1975. Each participant provided informed consent before participating in the study. Participants could continue their current medications at trial entry and throughout the course of the study as ordered by the treating physician. In addition, participants had to have a diagnosis of MS for at least one year before entering the study. Each participant was evaluated by the staff neurologist before enrollment in the study to verify the diagnosis of MS.

Inclusion and exclusion criteria

Inclusion criteria were (a) a diagnosis of MS for at least one year as established by the International Panel on MS Diagnosis McDonald Criteria (McDonald et al. 2001) and a score of at least 2.0 on the Kurtzke Expanded Disability Status Scale (EDSS) (Kurtzke 1983) signifying minimal disability in one functional system and at least one relapse within the previous year, (b) signed informed consent, (c) willingness and ability to consume oral dietary supplements, and (d) ability to drink sufficient water ($\geq$1 quart/100 pounds of body weight/day). Exclusion criteria were (a) concurrent enrollment in another study, (b) current hospitalization, (c) current pregnancy, or (d) inability or unwillingness to come to the MS center once per month to receive the dietary supplements, turn in the compliance measure, and complete follow-up testing.

Intervention

Participants were enrolled in an open-label, 12-month clinical trial. The broad-spectrum dietary supplement regimen used in this study consisted of polysaccharides and other nutrients that have been sold by commercial entities for more than 20 years. In addition, these products were collectively used as the study intervention to support cellular communication, neuronal synthesis, oxygen uptake, normal blood sugar levels, carbohydrate utilization, hormone balance, and antioxidation, among others. The following products were taken by each participant in this study: Classic Ambrotose, Lecithin, Empact, and Phytaloe (1 teaspoon three times per day of each) and Sport, Plus, Ambrotose AO, and Catalyst (1 capsule or tablet three times per day of each). The dietary supplements were provided to participants monthly at the MS center.

Outcomes and assessments

Each participant completed a basic demographic and medical history questionnaire at baseline. At each follow-up (3, 6, 9, and 12 months), participants were assessed for (a)

quality of life, (b) symptoms of disease severity, (c) functionality, (d) adverse reactions and compliance to the intervention, (e) basic medical and health status, and (f) current medications.

Assessment battery for severity of symptoms, functionality, and quality of life

The Functional Assessment of Multiple Sclerosis (FAMS; Cella et al. 1996) is an MS-specific quality of life instrument. The FAMS consists of 44 self-report scored items in six quality of life scales: mobility (seven items), symptoms (seven items), emotional well-being (seven items), general contentment (seven items), thinking/fatigue (nine items), and family/social well-being (seven items). The participant responds to each item for relevance in the previous seven days. Items are scored on a 5-point Likert scale ranging from 0 (not at all) to 4 (very much), with some items reverse-scored to enhance internal validity of the instrument. The instrument also has 15 items labeled as additional concerns that may provide useful information for clinicians. The FAMS has demonstrated adequate statistical validity (Cella et al. 1996) and the ability to predict disease disability progression (Benito-Leon et al. 2013).

The EQ-5D-3L is a standardized instrument developed by the EuroQol Group to provide a simple, generic measure of health status (EuroQol Group 1990; Brooks 1996). The measure consists of two pages: the EQ-5D descriptive system and the EQ visual analog scale (VAS). The descriptive system has the following five dimensions: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each dimension has three levels: no problems, some problems, and extreme problems. The descriptive system (i.e., health states) can also be converted into a single summary Index Value by applying a formula that attaches values to each of the levels in each dimension (Shaw et al. 2005). The Index Value can be calculated by deducting the appropriate weights from 1, the value for full health. The EQ VAS records the respondent's self-rated health on a vertical, visual scale, where the endpoints are labeled "Best imaginable health state" and "Worst imaginable health state."

The Beck Depression Inventory-II (Beck et al. 1996) was administered to assess changes in depressive symptoms over the course of the intervention. The BDI consists of 21 items and is scored 0 to 63, where higher levels indicate progressive levels of depression (0-9: minimal, 10-18: mild, 19-29: moderate, and 30-63: severe).

The 100-item Health Conditions Discomfort Scale (HCDS) was designed by the MS center to provide an overall patient symptom assessment. The items pertain to problems associated with the skin, head, hair and nails, eyes, ears, nose and sinuses, mouth and throat, neck, chest/underarm, lungs, heart, veins and arteries in arms and legs, kidneys and bladder, genitals, muscles, joints, and ligaments, nerves, thyroid, hormones, blood, and general. Items are scored from 0 "no problem" to 10 "severe." Individual scores are summed to obtain a total score.

The 50-item Self-Assessment of Severity of MS Symptoms Scale (SASMSSS) was designed by the MS center to provide an assessment of specific physical and psychological symptoms. The items pertain to scales for abnormal sensations, visual disturbances, motor sensations, psychological and neurological symptoms, cognitive symptoms, and sleep disturbances. Items are scored from 0 "none" to 10 "the worst."

Statistical analysis

Data were analyzed using SPSS 24 (IBM Inc., Chicago, IL) for Windows. Frequency and descriptive statistics were calculated on all variables. We used repeated-measures analysis of variance (ANOVA) to examine the effect of time on the FAMS, EQ-5D-3L, BDI, HCDS, and SASMSSS. A statistically significant main effect of time was further examined using simple effects pairwise t tests. We used the $\acute{\omega}$ Huynh-Feldt correction factor to adjust the degrees of freedom for the within-subjects effect for the test of significance. The criterion for statistical significance for all tests was $\alpha = 0.05$.

Results

Sociodemographics

Seven females and eight males enrolled in the study with an average age of 51.3 years (SD = 7.2; R = 38, 65). Participants had been diagnosed with RRMS for an average of 12.4 years (SD = 7.4; R = 2, 25). The mean baseline EDSS score was 4.1 (SD = 1.9, R = 2.0, 9.0). Participants were taking the following MS medications: Tysabri ($n = 7$), Betaseron ($n = 5$), intravenous immunoglobulin ($n = 2$), and no disease-modifying therapy (DMT) per choice ($n = 1$).

Tolerability

Two participants reported having an increase in soft stools upon starting the intervention. Four participants reported having nausea and vomiting in response to taking the dietary supplements, although all of them had previously reported the same symptoms. In addition, several participants with unusually high pill burdens (>10 medications per day) noted difficulty in taking the products.

Severity of symptoms, functionality, and quality of life

See Table 1 for the descriptive statistics, the main ANOVA effect for time, and the $\acute{\omega}$ Huynh-Feldt correction factor for the within-subjects effect for all FAMS scales. For the

Table 1. The FAMS scales at baseline and after 12 months of a polysaccharide-based multinutrient dietary supplement.

Variable	Baseline	3 Months	6 Months	9 Months	12 Months	F statistic for main effect
Mobility*	12.0 ± 5.9	14.7 ± 6.7	13.9 ± 6.3	15.9 ± 6.1	14.3 ± 6.7	F = 4.2, $p = 0.01$, CF = 0.79
Symptoms*	17.0 ± 3.7	21.9 ± 4.0	21.1 ± 5.1	23.1 ± 3.6	23.9 ± 3.3	F = 9.6, $p < 0.001$, CF = 0.62
Emotional well-being	20.3 ± 4.3	21.3 ± 4.2	22.0 ± 4.8	22.7 ± 4.9	21.7 ± 5.2	F = 2.4, $p = 0.065$, CF = 1.0
General contentment°	15.1 ± 6.2	16.9 ± 6.5	16.1 ± 6.4	18.7 ± 6.9	16.9 ± 6.5	F = 3.0, $p = 0.03$, CF = 0.89
Thinking and fatigue#	16.1 ± 6.6	21.7 ± 5.3	22.9 ± 6.4	25.6 ± 4.7	23.3 ± 5.6	F = 11.1, $p < 0.001$, CF = 0.99
Family/social well-being	17.9 ± 6.8	20.7 ± 7.0	20.0 ± 6.5	21.1 ± 5.7	19.7 ± 5.7	F = 1.9, $p = 0.16$, CF = 0.67
Total#	98.3 ± 25.4	117.2 ± 23.5	116.1 ± 24.7	127.1 ± 23.3	119.7 ± 24.7	F = 13.6, $p < 0.001$, CF = 0.84
Additional concerns#	33.4 ± 6.4	37.9 ± 5.5	39.1 ± 8.0	41.5 ± 7.1	38.9 ± 6.8	F = 8.6, $p < 0.001$, CF = 1.0

FAMS, Functional Assessment of Multiple Sclerosis; CF, $\acute{\omega}$ Huynh-Feldt correction factor. Values are displayed as mean- ± standard deviation, and higher scores indicate improvement.
*Baseline value was significantly ($p < 0.05$) lower than values at 3, 9, and 12 months.
°Baseline value was significantly ($p < 0.05$) lower than value at 9 months.
#Baseline value was significantly ($p < 0.05$) lower than values at 3, 6, 9, and 12 months.

FAMS Mobility scale, the main effect for time was significant ($p = 0.01$). Pairwise comparisons revealed that the baseline value was significantly lower than the values at 3 months (M difference = 3.1; SE = 1.3, 95% CI = 0.3 to 5.9, $p = 0.03$), 9 months (M difference = 3.8; SE = 1.3, 95% CI = 0.9 to 6.7, $p = 0.01$), and 12 months (M difference = 2.3; SE = 1.0, 95% CI = 0.1 to 4.5, $p = 0.05$). For the FAMS Symptoms scale, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly lower than the values at 3 months (M difference = 5.5; SE = 1.0, 95% CI = 0.3 to 7.6, $p = 0.03$), 9 months (M difference = 6.2; SE = 1.2, 95% CI = 3.6 to 8.8, $p < 0.001$), and 12 months (M difference = 6.9; SE = 1.1, 95% CI = 4.6 to 9.2, $p < 0.001$). For the FAMS General Contentment scale, the main effect for time was significant ($p = 0.03$). Pairwise comparisons revealed that the baseline value was significantly lower than the value at 9 months (M difference = 3.6; SE = 1.3, 95% CI = 0.7 to 6.4, $p = 0.02$). For the FAMS Thinking and Fatigue scale, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly lower than the values at 3 months (M difference = 5.9; SE = 1.5, 95% CI = 2.6 to 9.1, $p = 0.002$), 6 months (M difference = 6.5; SE = 1.9, 95% CI = 2.4 to 10.6, $p = 0.01$), 9 months (M difference = 9.4; SE = 1.5, 95% CI = 6.1 to 12.8, $p < 0.001$), and 12 months (M difference = 6.9; SE = 1.6, 95% CI = 3.3 to 10.4, $p = 0.001$). For the FAMS Total, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly lower than the values at 3 months (M difference = 20.5; SE = 4.1, 95% CI = 11.7 to 29.2, $p < 0.001$), 6 months (M difference = 16.6; SE = 5.8, 95% CI = 4.1 to 29.2, $p = 0.01$), 9 months (M difference = 28.6; SE = 4.3, 95% CI = 19.2 to 37.9, $p < 0.001$), and 12 months (M difference = 21.6; SE = 3.6, 95% CI = 13.7 to 29.4, $p < 0.001$). For the FAMS Additional Concerns, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly lower than the values at 3 months (M difference = 5.1; SE = 1.6, 95% CI = 1.6 to 8.5, $p = 0.01$), 6 months (M difference = 5.7; SE = 1.5, 95% CI = 2.5 to 8.9, $p = 0.002$), 9 months (M difference = 8.1; SE = 1.8, 95% CI = 4.4, to 11.9, $p < 0.001$), and 12 months (M difference = 5.8; SE = 1.1, 95% CI = 3.4 to 8.2, $p < 0.001$). The effects for Emotional Well-Being and Family/Social Well-Being were nonsignificant.

See Table 2 for the descriptive statistics, the main ANOVA effect for time, and the $\acute{\omega}$ Huynh-Feldt correction factor for the within-subjects effect for the EQ-5D-3L VAS and Index Value. For the VAS, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly lower than the values at 3 months (M difference = 17.6; SE = 4.9, 95% CI = 7.1 to 28.2, $p = 0.01$), 6 months (M difference = 20.4; SE = 4.9, 95% CI = 10.0 to 30.9, $p = 0.001$), 9 months (M difference = 19.1; SE = 5.4, 95% CI = 7.5 to 30.7, $p = 0.01$), and 12 months

Table 2. The EQ-5D-3L VAS and index value at baseline and after 12 months of a polysaccharide-based multinutrient dietary supplement.

Variable	Baseline	3 Months	6 Months	9 Months	12 Months	F statistic for main effect
VAS[#]	40.9 ± 20.0	58.5 ± 15.5	61.3 ± 17.1	60.0 ± 20.4	63.0 ± 21.6	F = 7.9, $p < 0.001$, CF = 0.87
Index value[*]	0.61 ± 0.18	0.69 ± 0.19	0.68 ± 0.22	0.72 ± 0.19	0.73 ± 0.21	F = 4.7, $p = 0.01$, CF = 0.86

VAS, visual analog scale; CF, $\acute{\omega}$ Huynh-Feldt correction factor. Values are displayed as mean ± standard deviation, and higher scores indicate improvement.

[*]Baseline value was significantly ($p < 0.05$) lower than values at 3, 9, and 12 months.

[#]Baseline value was significantly ($p < 0.05$) lower than values at 3, 6, 9, and 12 months.

Table 3. Percentage of the level of problem by dimension of the EQ-5D-3L at baseline and after 12 months of a polysaccharide-based multinutrient dietary supplement.

Variable	Level of problem	Baseline	3 Months	6 Months	9 Months	12 Months
Mobility	None	0.0	20.0	26.7	6.7	21.4
	Some	93.3	73.3	66.7	86.7	71.4
	Extreme	6.7	6.7	6.7	6.7	7.1
Self-care	None	53.3	53.3	73.3	60.0	71.4
	Some	40.0	40.0	20.0	33.3	21.4
	Extreme	6.7	6.7	6.7	6.7	7.1
Usual activities	None	13.3	33.3	33.3	46.7	42.9
	Some	73.3	60.0	53.3	46.7	50.0
	Extreme	13.3	6.7	13.3	6.7	7.1
Pain/discomfort	None	6.7	13.3	26.7	26.7	42.9
	Some	80.0	86.7	66.7	73.3	57.1
	Extreme	13.3	0.0	6.7	0.0	0.0
Anxiety/depression	None	33.3	53.3	53.3	66.7	57.1
	Some	66.7	46.7	40.0	33.3	42.9
	Extreme	0.0	0.0	6.7	0.0	0.0

Values are percentage of the sample with the level of problem at each timepoint by dimension.

Table 4. The BDI and HCDS at baseline and after 12 months of a polysaccharide-based multinutrient dietary supplement.

Variable	Baseline	3 Months	6 Months	9 Months	12 Months	F statistic for main effect
BDI^{+}	14.9 ± 9.7	9.1 ± 6.9	7.1 ± 5.5	7.2 ± 7.2	8.9 ± 8.6	F = 7.2, p = 0.001, CF = 0.65
HCDS^{+}	179.8 ± 99.9	97.3 ± 55.1	78.9 ± 54.6	76.3 ± 69.1	73.1 ± 55.8	F = 13.7, $p < 0.001$, CF = 0.40

BDI, Beck Depression Inventory; HCDS, Health Conditions Discomfort Scale; CF, $\acute{\omega}$ Huynh-Feldt correction factor. Values are displayed as mean ± standard deviation, and lower scores indicate improvement.
$^{+}$Baseline value was significantly ($p < 0.05$) higher than values at 3, 6, 9, and 12 months.

(M difference = 22.2; SE = 6.1, 95% CI = 9.0 to 35.2, $p = 0.01$). For the Index Value, the main effect for time was significant ($p = 0.01$). Pairwise comparisons revealed that the baseline value was significantly lower than the values at 3 months (M difference = 0.10; SE = 0.04, 95% CI = 0.02 to 0.18, $p = 0.02$), 9 months (M difference = 0.12; SE = 0.04, 95% CI = 0.04 to 0.20, $p = 0.04$), and 12 months (M difference = 0.13; SE = 0.05, 95% CI = 0.03 to 0.23, $p = 0.02$).

See Table 3 for the EQ-5D-3L health profile by reported proportion of each level of dimension by timepoint (i.e., Level 1 = no problem, Level 2 = some problem, and Level 3 = extreme problem). For Mobility, no participants reported no problems at baseline, but 21% reported no problems at 12 months. For Self-Care, 53% of participants reported no problems at baseline, while 71% reported no problems at 12 months. For Usual Activities, 13% reported no problems at baseline, while 43% reported no problems at 12 months. For Pain/Discomfort, 7% of participants reported no problem at baseline, while 43% reported no problems at 12 months. For Anxiety/Depression, 33% reported no problem at baseline, while 57% reported no problems at 12 months.

See Table 4 for the descriptive statistics, the main ANOVA effect for time, and the $\acute{\omega}$ Huynh-Feldt correction factor for the within-subjects effect for the BDI and HCDS. For the BDI, the main effect for time was significant ($p = 0.001$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 3 months (M difference = 5.9; SE = 2.0, 95% CI = 1.55 to 10.19, $p = 0.01$), 6 months (M difference = 7.8; SE = 2.4, 95% CI = 2.65 to 12.9, $p = 0.006$), 9 months (M difference = 7.7; SE = 2.1, 95% CI = 3.14 to 12.3, $p = 0.003$), and 12 months (M difference = 6.0; SE = 2.2, 95% CI = 1.25 to 10.8, $p = 0.02$). For the HCDS, the main effect for time was significant

($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 3 months (M difference = 82.5; SE = 20.4, 95% CI = 38.6 to 126.3, $p = 0.001$), 6 months (M difference = 100.9; SE = 25.9, 95% CI = 45.4 to 156.4, $p = 0.002$), 9 months (M difference = 103.5; SE = 27.6, 95% CI = 44.2 to 162.7, $p = 0.002$), and 12 months (M difference = 106.7; SE = 22.4, 95% CI = 58.7 to 154.8, $p < 0.001$).

See Table 5 for the descriptive statistics, the main ANOVA effect for time, and the $\acute{\omega}$ Huynh-Feldt correction factor for the within-subjects effect for all the SASMSSS scales. For the SASMSSS Abnormal Sensations scale, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 3 months (M difference = 1.1; SE = 0.4, 95% CI = 0.3 to 1.9, $p = 0.01$), 6 months (M difference = 1.2; SE = 0.5, 95% CI = 0.2 to 2.2, $p = 0.03$), 9 months (M difference = 1.7; SE = 0.4, 95% CI = 0.9 to 2.6, $p = 0.001$), and 12 months (M difference = 1.8; SE = 0.4, 95% CI = 1.0 to 2.5, $p < 0.001$). For the SASMSSS Visual Disturbances scale, the main effect for time was significant ($p = 0.01$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 3 months (M difference = 1.0; SE = 0.3, 95% CI = 0.4 to 1.6, $p = 0.01$), 6 months (M difference = 0.9; SE = 0.3, 95% CI = 0.2 to 1.7, $p = 0.02$), 9 months (M difference = 1.0; SE = 0.4, 95% CI = 0.3 to 1.8, $p = 0.01$), and 12 months (M difference = 1.2; SE = 0.3, 95% CI = 0.5 to 1.9, $p = 0.01$). For the SASMSSS Motor Sensations scale, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 3 months (M difference = 1.4; SE = 0.4, 95% CI = 0.5 to 2.2, $p = 0.01$), 6 months (M difference = 1.7; SE = 0.4, 95% CI = 0.8 to 2.6, $p = 0.001$), 9 months (M difference = 1.9; SE = 0.3, 95% CI = 1.2 to 2.6, $p < 0.001$), and 12 months (M difference = 1.7; SE = 0.3, 95% CI = 1.0 to 2.4, $p < 0.001$). For the SASMSSS Psychological and Neurological Sensations scale, the main effect for time was significant ($p = 0.01$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 3 months (M difference = 1.6; SE = 0.4, 95% CI = 0.6 to 2.5, $p = 0.01$), 6 months (M difference = 1.5; SE = 0.6, 95% CI = 0.1 to 2.9, $p = 0.03$), 9 months (M difference = 2.0; SE = 0.5, 95% CI = 0.8 to 3.2, $p = 0.01$), and 12 months (M difference = 1.8; SE = 0.5, 95% CI = 0.6 to 2.9, $p = 0.01$). For the SASMSSS Cognitive Symptoms scale, the main effect for time was significant ($p < 0.001$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 3 months (M difference = 1.7; SE = 0.5, 95% CI = 0.6 to 2.8, $p = 0.01$), 6 months (M difference = 1.7; SE = 0.5, 95% CI = 0.5 to 2.8, $p = 0.01$), 9 months (M difference = 2.0; SE = 0.5, 95% CI = 1.0 to 2.9, $p = 0.001$), and 12 months (M difference = 1.6; SE = 0.5, 95% CI = 0.6 to 2.6, $p = 0.01$). For the SASMSSS Sleep Disturbances scale, the main effect for time was significant ($p = 0.01$). Pairwise comparisons revealed that the baseline value was significantly higher than the values at 6 months (M difference = 1.5; SE = 0.5, 95% CI = 0.3 to 2.6, $p = 0.02$), 9 months (M difference = 1.6; SE = 0.5, 95% CI = 0.6 to 2.7, $p = 0.01$), and 12 months (M difference = 1.6; SE = 0.5, 95% CI = 0.6 to 2.7, $p = 0.01$).

Discussion

MS patients endure a heavy burden of disability, including (a) ataxia, (b) mood disorders, (c) cognitive and visual disturbances, (d) bladder and bowel dysfunction,

Table 5. The SASMSSS scales at baseline and follow-up.

Variable	Baseline	3 Months	6 Months	9 Months	12 Months	F statistic for main effect
Abnormal sensations[+]	3.2 ± 1.4	2.3 ± 1.3	2.1 ± 1.8	1.5 ± 1.4	1.5 ± 1.4	F = 7.6, $p < 0.001$, CF = 1.0
Visual disturbances[+]	2.1 ± 1.7	1.3 ± 1.2	1.2 ± 1.4	1.1 ± 1.3	1.0 ± 1.0	F = 3.8, $p = 0.01$, CF = 0.95
Motor sensations[+]	3.8 ± 1.4	2.5 ± 1.4	2.2 ± 1.5	2.0 ± 1.4	2.2 ± 1.6	F = 13.2, $p < 0.001$, CF = 0.83
Psychological and neurological symptoms[+]	2.7 ± 2.3	1.2 ± 1.0	1.3 ± 1.7	0.9 ± 0.9	1.1 ± 1.2	F = 7.0, $p = 0.01$, CF = 0.59
Cognitive symptoms[+]	2.9 ± 1.8	1.3 ± 1.1	1.2 ± 1.6	1.0 ± 0.9	1.2 ± 1.4	F = 7.1, $p < 0.001$, CF = 0.86
Sleep disturbances[!]	2.7 ± 1.8	1.7 ± 1.8	1.2 ± 1.5	1.0 ± 1.1	1.1 ± 1.2	F = 6.2, p = 0.01, CF = 0.62

SASMSSS, Self-Assessment of Severity of MS Symptoms Scale; $\acute{\omega}$ Huynh-Feldt CF, correction factor. Values are displayed as mean ± standard deviation, and lower scores indicate improvement.

[+]Baseline value was significantly ($p < 0.05$) higher than values at 3, 6, 9, and 12 months.

[!]Baseline value was significantly ($p < 0.05$) higher than values at 6, 9, and 12 months.

(e) fatigue, and (f) impaired activities of daily living (Ford et al. 2001). DMTs are used to modify the course of the disease, reduce clinical exacerbations, decrease debility, and enhance the patient's quality of life. However, with treatment comes the significant issues of tolerability and safety. Because of the wide range of adverse DMT effects and lack of curative outcome, MS patients have expanded their use of other therapies, including dietary supplements (Leong et al. 2009).

Multiple improvements in quality of life, symptom of disease severity, and functionality were noted in the current study. Thinking and fatigue, mobility, and symptoms according to the FAMS and psychological and neurological sensations and cognitive symptoms according to the SASMSSS were significantly better. Global quality of life according to both the VAS and Index Value of the EQ-5D-3L and the overall score on the HCDS also significantly improved. The EQ-5D-3L is one of the most used health-related quality of life instruments in clinical trials (Brooks et al. 2003; Kiadaliri and Englund 2016). The baseline Index Value of our sample (0.61) was comparable to a study in Australia of MS patients (0.53; 95% CI, 0.38 to 0.43; Ahmad et al. 2017), but by 12 months our participants had increased to 0.73. These findings are important as currently available pharmacotherapies ameliorate the physical aspects of disease, but do not fare as well in improving quality of life (Zwibel and Smrtka 2011). Quality of life measures not only a person's contentment, but also the ability to function and live productively (World Health Organization 1998). MS patients have significantly reduced quality of life compared to healthy people and those with epilepsy, diabetes, and rheumatoid arthritis (Pittock et al. 2004; Zernicke et al. 2013; Mikula et al. 2015). Fatigue is one of the most common symptoms of MS (70%-90%), with a marked negative effect on quality of life (Surakka et al. 2004; Neill et al. 2006). MS patients report fatigue as the worst and most debilitating symptom of the disorder, affecting energy, cognitive function, and motor abilities and undermining their ability to cope with the disease (Pittion-Vouyovitch et al. 2006; Kalron 2015). We are unaware of other dietary supplement intervention trials showing significant improvement of these debilitating symptoms in MS patients.

Evidence suggests that one pathologic process of MS includes the elimination of lower motor neurons and lower compound muscle action potential, which is correlated with muscle strength and motor unit count (Vogt et al. 2009). Such deficits lead to higher EDSS scores. Our participants reported improvements according to both the EQ-5D-3L and FAMS, which contain questions about lower limb mobility function. Thus, the current dietary supplement regimen may counteract some negative effects on quality of life of diminished mobility in MS patients.

In addition, depressive symptoms according to the BDI, anxiety and depression on the EQ-5D-3L, and emotional well-being on the FAMS all significantly improved over the 12-month intervention. Mood disorders (i.e., depression and anxiety) are highly prevalent in the MS population, particularly after the initial phase of the disorder (Janssens et al. 2006; Giordano et al. 2011; Tan-Kristanto and Kiropoulos 2015). The lifetime prevalence rates of depression in MS patients are between 15% and 50% (Sadovnick et al. 1991; Siegert and Abernethy 2005). Because depression is so common, has substantial illness-related burden similar to cardiovascular disease, and is a leading cause of disability itself (World Health Organization et al. 2004; Eby and Eby 2010),

methods to counteract mood disorder are crucial. Various nutrients, including inositol (Levine et al. 1995) and S-adenosylmethionine (Bell et al. 1988), have been used in clinical trials and show modest, short-term improvements in depressive symptoms. We also recently found a minor effect of intravenous magnesium sulfate on quality of life symptoms in patients with treatment-resistant depression (Mehdi et al. 2017). Thus, our approach, using a broad-spectrum dietary supplement regimen to support various physiologic targets, may represent an effective nonpharmacologic alternative to conventional treatment of MS-associated depression.

Limitations

Several limitations are noted in this study. A future study could be conducted with a double-blind placebo control and post intervention follow-up sessions to determine whether the results in the current study are supported with a more rigorous design. The dietary supplement regimen has a wide variety of polysaccharides, phytonutrients, vitamins, and minerals, making it impossible to delineate those nutrients that may be most responsible for the effects shown in the study. Although the staff qualitatively questioned participants about dietary habits, no structured assessment of food consumption was used, so no effect of overall diet can be considered. Study assessors were not blinded to the study participants, but they assessed participants for all studies occurring simultaneously, so their influence on this study should have been no different than on any other. It was not possible to objectively determine compliance with the protocol as these products do not readily lend themselves to metabolite analysis. We did not restrict or change the use of medications by our participants, given the ethical considerations associated with such decision. Nonetheless, because participants were taking different MS medications or no therapy in the case of one participant, this could be a confounding factor in the results of the study. Finally, this study had a small sample size, so the findings from a larger group of participants are unknown.

Conclusions

MS affects millions of people worldwide without a known cure. The broad-spectrum dietary supplement regimen used in the current study resulted in significant and consistent improvements in quality of life, functionality, and symptom of disease severity on validated measures. The mechanisms by which our dietary supplement regimen influenced the clinical findings need further study with a larger sample size. The current findings indicate that this supplement regimen may have a major effect on improving quality of life in MS patients, a prospect with far-reaching clinical and fiscal implications.

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Data availability statement

The data that support the findings of this study are available from the corresponding author, (JEL), upon reasonable request.

Declaration of interest

H. Reginald McDaniel has received income as a seller of the dietary supplements used in this study. Christopher LaGanke, Laura Bloom, Sharon Goldberg, Judith Hensel, Laura A. Lantigua, Lucas C. Lages, Steven E. Atlas, Judi M. Woolger, and John E. Lewis have no conflicts of interest to report.

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