

The Effectiveness of Modified Mediterranean and Traditional Persian Diets in Fatigue and Depressive Severity in People with Multiple Sclerosis: A Randomized Controlled Clinical Trial

Mohammad Hossein Sharifi^{1,2}, MD, PhD, MPH;  Maryam Poursadeghfard³, MD; Maryam Afshari², MD; Zahra Alizadeh⁴, MSc; Mohammad Vatanpour⁵, MSc; Mitra Soltani^{4,6}, MSc; Hossein Molavi Vardanjani¹, PhD, MPH; Amir Mohammad Jaladat¹, MD, PhD, MPH; Majid Nimrouzi¹, MD, PhD, MPH 

¹Research Center for Traditional Medicine and History of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran;

²Non-Communicable Diseases Research Center, School of Medicine, Shiraz University of Medical Sciences, Shiraz, Iran;

³Clinical Neurology Research Center, Shiraz University of Medical Sciences, Shiraz, Iran;

⁴Imam Reza Specialized and Subspecialized Polyclinic, Shiraz University of Medical Sciences, Shiraz, Iran;

⁵Master Student of Nutrition Sciences, Department of Clinical Nutrition, School of Nutrition and Food Sciences, Shiraz University of Medical Sciences, Shiraz, Iran;

⁶Department of Clinical Nutrition, Tehran University of Medical Sciences, Tehran, Iran

Correspondence:

Majid Nimrouzi, MD, PhD, MPH;
Shiraz School of Medicine, Imam Hossein Sq., Zand Blvd., Postal code: 71348-45794, Shiraz, Iran

Tel: +98 71 32084028

Email: mnimrouzi@yahoo.com

Received: 10 March 2024

Revised: 16 May 2024

Accepted: 11 June 2024

What's Known

- There is a lack of scientific understanding of diet intervention's potential in managing multiple sclerosis (MS). As far as we know, few studies have been conducted to investigate the effect of traditional Persian food (hot, cold, or balanced food) and Mediterranean diet interventions on fatigue and depression in MS.

What's New

- Adhering to the Mediterranean diet can alleviate fatigue scores in MS patients while having no effect on the depression score. In contrast, adhering to the traditional Persian diet recommendation can reduce depression scores without affecting fatigue scores in MS patients.

Abstract

Background: Research into managing depression and fatigue, two typical symptoms of multiple sclerosis (MS), is constantly expanding. This study aimed to assess the efficacy of the modified Mediterranean (MED) diet or the Traditional Persian (TP) diet in terms of fatigue and depression severity in patients with MS.

Methods: In this single-center, single-blind, randomized clinical trial, 90 patients were enrolled. The patients were randomly assigned to either the MED or TP diet intervention and control groups for two months between July 2022 and February 2023, in Shiraz, Iran. The Krupp Questionnaire for Fatigue Severity Scale and the Beck Depression questionnaire were used. The Chi square test, Kruskal-Wallis test, One-way ANOVA, and backward elimination technique were employed. STATA statistical software (version 17) was utilized for data analysis. $P \leq 0.05$ was considered statistically significant.

Results: The mean age of 90 participants was 35.64 ± 9.12 , and 82.2% were women. The analysis revealed a negative correlation between fatigue severity and MED diet intervention ($-4.17 [-8.18-0.16]$; $P=0.04$). However, there was no association between fatigue severity and TP diet intervention ($-3.82 [-7.96, 0.32]$; $P=0.07$).

The analysis showed that there was a statistically significant relationship between lower depression scores and TP diet intervention ($-2.89 [-5.59, -0.19]$; $P=0.03$). However, there was no association between depression scores and MED diet intervention ($P=0.22$). Lower depression score was also associated with older age and higher socioeconomic status ($P=0.002$ and $P=0.006$). It was also shown that longer duration of disease ($P=0.05$) and higher fatigue severity ($P=0.001$) were associated with higher depression scores.

Conclusion: Adhering to the MED diet could reduce fatigue scores in MS patients while having no effect on the depression score. In contrast, adhering to the TP diet recommendation could reduce depression scores without affecting fatigue scores in MS patients.

Trial registration number: IRCT20181113041641N1.

Please cite this article as: Sharifi MH, Poursadeghfard M, Afshari M, Alizadeh Z, Vatanpour M, Soltani M, Molavi Vardanjani H, Jaladat AM, Nimrouzi M. The Effectiveness of Modified Mediterranean and Traditional Persian Diets in Fatigue and Depressive Severity in People with Multiple Sclerosis: A Randomized Controlled Clinical Trial. Iran J Med Sci. 2025;50(3):146-158. doi: 10.30476/ijms.2024.101961.3472.

Keywords • Fatigue • Depression • Mediterranean diet • Multiple sclerosis • Persian traditional medicine

research indicated that hot-natured food could improve clinical scores of MS and depression by increasing cytokines such as interleukin 4.^{18, 33} These findings are somewhat astonishing, given that previous studies showed that foods high in vitamin B12 and folate can help with depression.^{34, 35} However, Xie conducted a study and found that cold-natured foods are high in vitamin B12 and folate.¹⁶ Thus, these findings should be interpreted with caution. Furthermore, a lack of association between depression scores and MED diet intervention was an unexpected finding. Previous research found an inverse significant association between adherence to the MED diet and depression in cross-sectional and intervention studies; while, no significant association was found in cohort studies.^{36, 37} This discrepancy could be attributed to the small sample size of the trials and the short intervention duration.

The present study found a statistically significant relationship between increasing fatigue severity and higher depression scores. This finding was consistent with that of a previous study which reported that fatigue and depression were highly correlated in people with MS.³⁸ Furthermore, Lee's study found that depression and fatigue were associated with increased immune system activation, which might be an important target for treatment.³⁹

To the best of our knowledge, this is the first clinical trial that aimed to determine the impact of a TP diet (hot and cold pattern of food) on fatigue and the severity of depression in patients with MS. As a result, this topic could direct researchers' attention toward specific research areas. Additionally, the findings of this study can help healthcare providers and specialists to guide the questions of MS patients regarding the relationship between TD and MD diet in relieving the symptoms of fatigue and depression. Although this study provided some preliminary insight into the potential role of TP dietary interventions in the management of depression and fatigue in patients with MS, it had several limitations. The energy and macro/micronutrient intakes, phase of MS, use of medications, and nature of the entire diet were some of the limitations of the present study. The primary focus of this study was on people with MS. Thus, more research is required to determine the long-term safety and the safety of TP diet intervention among patients with other autoimmune diseases.

Conclusion

The findings of the present study indicated that

adhering to the MED diet for 2 months could reduce fatigue scores in people with MS while having no effect on the depression score. In contrast, adhering to the TP diet recommendation could reduce depression scores without affecting fatigue scores in patients with MS. Since the underlying causes of fatigue and depression in MS patients are unknown, a more thorough investigation of the relationship between dietary intervention and MS progression and symptom improvement is recommended.

Acknowledgment

The authors would like to thank Shiraz University of Medical Sciences, Shiraz, Iran, and also the Center for Development of Clinical Research of Nemazee Hospital and Dr. Amir Yousef Farahmandi for editorial assistance.

Authors' Contribution

MH.Sh: Study concept, study design, data gathering, and drafting; M.P: Study concept, drafting, and reviewing; M.A: Data gathering and drafting; Z.A: Data gathering, and drafting; M.V: Data gathering, and drafting; M.S: Data gathering, and drafting; H.MV: Study design, data interpretation, and drafting; AM.J: Data gathering, and drafting; M.N: Data gathering and drafting; All authors read and approved the final manuscript and agreed to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

Conflict of Interest: None declared.

References

- 1 McGinley MP, Goldschmidt CH, Rae-Grant AD. Diagnosis and Treatment of Multiple Sclerosis: A Review. *JAMA*. 2021;325:765-79. doi: 10.1001/jama.2020.26858. PubMed PMID: 33620411.
- 2 Razeghi-Jahromi S, Doosti R, Ghorbani Z, Saeedi R, Abolhasani M, Akbari N, et al. A randomized controlled trial investigating the effects of a mediterranean-like diet in patients with multiple sclerosis-associated cognitive impairments and fatigue. *Curr J Neurol*. 2020;19:112-21. doi: 10.18502/cjn.v19i3.5424. PubMed PMID: 38011378; PubMed Central PMCID: PMC8185587.
- 3 Marchesi O, Vizzino C, Filippi M, Rocca MA. Current perspectives on the diagnosis and management of fatigue in multiple sclerosis.