Study Protocol: Role of Intermittent Fasting on Disease Severity and Quality of Life in Psoriasis and Psoriatic Arthritis: A Single-Blind Parallel Group Randomized Control Trial

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Abstract

BACKGROUND Psoriasis and psoriatic arthritis (PsA) have a strong association with obesity and metabolic syndrome. Despite patient interest in non-pharmacologic methods to treat psoriasis and manage overall health, there is insufficient data available to guide dietary counseling. **OBJECTIVE** This study aims to identify the role of a popular anti-inflammatory diet known as intermittent fasting (IF) in psoriasis and psoriatic arthritis (PsA). **METHODS** A single-blind parallel group randomized control trial will be performed in 60 patients who have been diagnosed with psoriasis or PsA. Patients will be assigned 1:1 to either the IF group or control group. Patients assigned to the IF group will follow a 16:8 fasting IF method for the first 12 weeks, followed by the resumption of their routine diet. Patients assigned to the control group will follow their routine diet for 24 weeks. **RESULTS** A total of 24 patients have been enrolled in our study, with a final enrollment goal of 60 patients. The final visit is foreseen for July 2023. **CONCLUSIONS** This study aims to identify the role of a popular anti-inflammatory diet known as intermittent fasting (IF) in the management of psoriasis and PsA. Publishing this data will allow all dermatologists and the National Psoriasis Foundation to provide a consistent, evidence-based recommendation for IF as a potential non-pharmacologic intervention for patients with psoriasis and psoriatic arthritis (PsA).

Keywords: psoriasis; psoriatic arthritis; intermittent fasting, dietary intervention

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INTRODUCTION

Psoriasis is a chronic inflammatory skin condition affecting 3.2% of U.S. adults. Psoriasis is known to have detrimental effects on quality of life.[1,2] While topical and systemic therapies are the current mainstays of treatment, patients and physicians have become increasingly interested in the role of diet on disease prevention and progression.[3] A 2017 survey revealed that 86% of patients with psoriasis attempted to adjust their diet to improve disease severity.[3] However, many of these dietary interventions have been driven by patients and weight-loss opinion leaders without rigid study in regard to intervention success and the effect on systemic inflammatory profiles. Research agrees that diet alone should not be used for psoriasis or PsA management, but diet can synergistically improve the effects of standard topical and systemic therapies.[1]

Many studies have shown positive effects of weight reduction on disease severity and quality of life in psoriasis.[1,2,4,5] Increased body mass index (BMI) is associated with increased risk of new-onset psoriasis, and higher BMIs are associated with increased severity of psoriasis at onset, measured by Psoriasis Area and Severity Index (PASI).[6] An additional cross-sectional study showed that the PASI score was positively correlated with all three measures of weight, including BMI, waist circumference, and waist-to-hip ratio.[7] It has been suggested that a component of the improved PASI score seen with weight loss is due to the higher relative dosing of systemic therapies.[6]

Based on a 2018 study published for the National Psoriasis Foundation Medical Board, several dietary recommendations were developed using data from 55 distinct research studies.[1] First, the foundation concluded that dietary weight reduction is beneficial for patients with psoriasis who are overweight. In addition, gluten-free diets were also weakly recommended for patients that have anti-gliadin antibodies, which are found ubiquitously in patients with celiac disease. Finally, vitamin D supplementation was exclusively recommended for patients who were deemed deficient by laboratory studies. All other dietary supplements and interventions had weak evidence.[1,8] Given that these recommendations only apply to specific patient subpopulations, there is a heightened need for large multi-centered clinical trials to accurately validate these studies and provide further recommendations.[1,4,9]

Research regarding the impact of diet on psoriasis and PsA is ongoing. The majority of dietary interventions alter calories consumed or types of food consumed. Intermittent fasting (IF), which alters the timing of consumption, has become a popular option in those seeking weight loss and decreased risk for diseases of aging such as cardiovascular disease, stroke, hypertension, and elevated fasting glucose. Still, little is known about IF's effects on psoriasis disease course and severity.[10-13] IF is an attractive diet option because it does not limit the types or quality of foods consumed. While caloric restriction and IF produce similar reduction in weight and improved insulin sensitivity, IF offers additional anti-inflammatory benefits, reduced oxidative stress, and circadian rhythm synchrony, which are advantageous for inflammatory conditions, such as psoriasis.[6,8,14]

The pathophysiology behind the influence of dietary interventions in dermatology is complex. Increased levels of keystone pro-inflammatory cytokines implicated in psoriasis, IL-17, IL-23, IL-6 and TNF- , are also seen at elevated levels in patients who are obese. This pathophysiology correlates clinically, as obesity is associated with increased psoriasis incidence, severity, and therapeutic failure.[6,8,14] Additionally, further evidence is emerging that elements of the skin follow circadian rhythms.[15] Taken together, the evidence surrounding obesity, inflammation, and circadian rhythms support the role of diet in psoriasis management. IF addresses all of the aforementioned elements, which likely potentiate positive effects on the management of psoriasis and PsA.

METHODS

Research Hypothesis

We aim to determine the feasibility of a larger study assessing the association between IF and disease severity and quality of life in patients with psoriasis and PsA using standardized assessments of disease severity, PASI, Investigator's Global Assessment (IGA), and Psoriatic Arthritis Response Criteria (PsARC), and quality of life, Dermatology Life Quality Index (DLQI) and Health-related Life Quality Index (HRQL). We expect the IF intervention to significantly improve psoriasis and PsA-specific clinical scores and patient-reported outcomes in our interventional cohort compared to the control group. Higher BMIs (BMI >25) are expected to correlate with a greater improvement in clinical outcomes in comparison to lower BMIs.

Primary Objective

The primary objective of this study is to determine the feasibility of a larger study that is properly powered, assessing disease severity of psoriasis and psoriatic arthritis in patients following IF compared to routine diet. We

will utilize the Psoriasis Area and Severity Index (PASI) and the Psoriatic Arthritis Response Criteria (PsARC) to monitor disease activity at baseline assessment, 12-week timepoint, and 24-week timepoint.

Secondary Objectives

The secondary objectives of this study include quality of life assessment, using the Dermatology Life Quality Index (DLQI) for psoriasis and the Health-Related Quality of Life (HRQL) score for PsA. Additionally, we will assess amount of skin involvement using percentage of body surface area (BSA) involvement. Overall disease activity will be assessed using the Investigator Global Assessment (IGA). For PsA patients, we will also record the presence of enthesitis and/or dactylitis. Nail Psoriasis Severity Index (NAPSI) will be utilized to monitor nail involvement in all patients. Biometric measurements including weight, height, BMI, and waist-to-hip ratio will be recorded.

Study Design

We will conduct a prospective, single-blind parallel group randomized control trial to test the effects of IF on disease severity in 60 adults with psoriasis or PsA. The total study duration will be 24 weeks. Randomization will be performed using Microsoft Excel, and patients will subsequently be consented and enrolled in the study using our secure web platform, REDCap. Patients will be assigned to either the intervention or control arm. Evaluations will include clinical, biometric, and patient-reported outcomes. In-person timepoint assessments will be at the 12- and 24-week timepoints, with a total study duration of 24 weeks.

Recruitment, Eligibility, and Randomization

Participants will be identified through an electronic medical record search for established patients within the Ohio State University Wexner Medical Center Department of Dermatology practice with a diagnosis of mild-to-moderate psoriasis. Patients will then be provided the study information and offered entry into the study. Patients in the control group will be offered entry into the intermittent fasting group after the completion of the study as an incentive to participate.

Patients will be considered eligible for the study if they meet the full inclusion and exclusion criteria. Patients undergoing or planning to undergo an alteration in baseline exercise habits, smoking habits, or alternative psoriasis therapies during the course of this study will not be eligible. Patients are not to have had any systemic changes in psoriasis therapy in the six weeks leading up to the study. The impact of comorbid inflammatory disorders on results will be considered during analysis.

Inclusion Criteria:

- 18 years of age and older
- Established patient at the clinical site with a diagnosis of mild to moderate plaque psoriasis despite treatment
- Ability to consent and follow dietary instructions
- Overweight (BMI $\geq$ 25)
- No change in psoriasis treatment for 6 weeks

Exclusion Criteria:

- Pregnancy and/or breastfeeding
- Insulin-dependent diabetes
- Severe heart, kidney, and liver disease
- Past history of an eating disorder
- Obesity due to an underlying medical condition
- Use of medical treatment for weight reduction

Following consent, the participants who meet the inclusion criteria will be block randomized by the presence of PsA and time in a 1:1 ratio to either the IF diet intervention or standard routine dietary guidance. Recruitment and block randomization will ensure at least 20% of each group contains patients with PsA. The assessing physician investigator will be blinded to the group assignment of each patient, although the research coordinator will not be blinded. Patients cannot reasonably be blinded to their assignment.

Study Interventions

For the IF group of the study, subjects will be permitted to eat food of any type and quantity for 8 hours of each day. Patients in the standard routine dietary guidance group are encouraged to continue their current diet while recording their first and last meal of the day until the first data collection. By doing this, we will ensure that there is a difference in total energy consumption time between the IF group and our controls. After the first 12 weeks of the study and subsequent data collection, patients will be permitted to resume their normal dietary habits for the remaining 12 weeks of the study.

Outcome Measures

Baseline assessment will consist of standard psoriasis parameters including BSA, PASI, and IGA; evaluation will be performed by a blinded physician. These parameters will be reassessed at 12-week and 24-week timepoints. In addition, on each visit, patient reported outcomes will be collected using the DLQI. Biometric measurements of weight, height, BMI, and waist-to-hip ratio will be recorded at baseline and at the 12- and 24-week timepoints. Dietary adherence will be assessed monthly electronically via video visit, and dietary guidance will be provided and reviewed at each visit by the research coordinator.

Sample Size Calculations

Sample size calculations were performed based on preliminary data showing differences in psoriasis scoring due to religious fasting demonstrating an effect size of -0.89 points change in PASI scoring and a standard error of 1.2.[16,17] Calculating the effect size with a power of 0.8 and an α of 0.05 would indicate that 48 patients need to be enrolled across two arms. Accounting for a likely dropout and lack of adherence rate of 25%, we will enroll a total of 60 patients across the two arms.

Statistical Analysis

Baseline demographic data will be compared using Student's unpaired t-testing or χ^2/Fisher Exact test as appropriate. The primary endpoint will be assessed by generalized linear mixed modeling (GLMM) with a random intercept. An intention-to-treat methodology will be utilized to analyze the results.

RESULTS

Active recruitment of patients began in July 2022, and the first patient was enrolled in August 2022. As of December 2022, we enrolled a total of 24 patients. The last patient visit is foreseen in July 2023, and results are expected to be published December 2023.

DISCUSSION

Our research group has demonstrated an extensive interest in non-pharmacologic management of chronic inflammatory skin disease. Our group recently published data surrounding the role of oral health factors on psoriasis disease severity, as oral infections and dental caries have been associated with psoriasis.[18] Specifically, diets associated with high sugar were implicated in worse oral health and consequently poorer control of psoriatic symptoms. Poor gum health and higher BMIs were associated with more severe psoriasis symptoms. The significant role of oral hygiene and dietary practices in psoriasis development and progression became evident.

This new data, combined with the known role of diet in psoriasis development and progression, influenced our group to further research the impact of dietary interventions. In addition, we followed up this study by assessing the role of various diet types in controlling another chronic inflammatory skin disorder known as hidradenitis suppuritiva. In this second study, diet was among the most popular choices for possible lifestyle intervention based on a cohort of 591 patients.[19] Consequently, dietary modification was associated with the most significant increases in both subjective and objective symptom improvement when compared to other modifications, such as smoking cessation. This study also further highlighted the inherent interest of patients in utilizing diet to help manage their skin disease. Overall, our data surrounding the role of diet in chronic inflammatory skin disorders supports that we are well-positioned to take the next step in developing a preliminary clinical trial to test the effect size of implementing a weight loss diet popularly known as intermittent fasting (IF).

A recent study analyzing the effect of Ramadan fasting on moderate-to-severe psoriasis found statistically significant improvements in both PASI and DLQI; the fasting period coincided with circadian rhythms.[16] The same research group identified improvements in PsA disease severity scales after adjusting for weight loss, a potential confounding factor.[17] This impact on both diseases was attributed to changes in T-cell number and activity.

Additional research suggests that IF reduces cytokine production and decreases the effects of Th17 cells, which have been heavily implicated in both psoriasis and PsA.[20]

Given the promising preliminary data surrounding the role of IF in the disease course of psoriasis and PsA, our study aims to determine if IF is a valid method for improving psoriasis and PsA disease severity. Dietary interventions are low-cost and generally safe methods for potentially decreasing disease severity, reducing medical comorbidities, and improving effects of standard psoriasis therapies.[1,8] Based on our study findings, we hope to provide a framework for further investigation into the role of IF in psoriasis and to further contribute to the establishment of well-defined dietary recommendations for patients with psoriasis and PsA.

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Conflicts of Interest: Ben Kaffenberger has performed research for Biogen, OnQuality, BMS, Merck, is a consultant for Biogen, Eli Lilly Co, Novartis, and Novocure, and has received honoraria from Elsevier and has research funding from the Dermatology Foundation and National Psoriasis Foundation.

Jessica Kaffenberger serves as a Principal investigator for Abbott, AbbVie, Celegene, Corrona, Incyte, Eli Lilly, Janssen, Kantar Health, Pfizer, Regeneron, and UCB.

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Abbreviations

IF	intermittent fasting
PsA	psoriatic arthritis
BMI	body mass index
PASI	psoriasis area and severity index
IL	interleukin
TNF	tumor necrosis factor
BSA	body surface area
PGA	physician global assessment
DLQI	dermatology life quality index
GLMM	generalized linear mixed modeling

Footnotes: The initial draft of the manuscript was written by Ashley Gray, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

REFERENCES

1. Ford AR, Siegel M, Bagel J, et al. Dietary recommendations for adults with psoriasis or psoriatic arthritis from the medical board of the National Psoriasis Foundation: A systematic review. *JAMA Dermatol.* 2018;154:934–950. https://doi.org/10.1001/jamadermatol.2018.1412
2. Takeshita J, Grewal S, Langan SM, et al. Psoriasis and comorbid diseases: Epidemiology. *J Am Acad Dermatol.* 2017;76:377–390. https://doi.org/10.1016/j.jaad.2016.07.064
3. Afifi L, Danesh MJ, Lee KM, et al. Dietary behaviors in psoriasis: Patient-reported outcomes from a U.S. national survey. *Dermatol Ther (Heidelb).* 2017;7:227–242. https://doi.org/10.1007/s13555-017-0183-4
4. Pona A, Haidari W, Kolli SS, et al. Diet and psoriasis. *Dermatol Online J.* 2019;25:13030/qt1p37435s. https://doi.org/10.5070/D3252042883
5. Fernández-Armenteros JM, Gómez-Arbonés X, Buti-Soler M, et al. Psoriasis, metabolic syndrome and cardiovascular risk factors: A population-based study. *J Eur Acad Dermatol Venereol.* 2019;33:128–135. https://doi.org/10.1111/jdv.15159
6. Shelling ML, Kirsner RS. Gaining insights into the relationship of obesity, weight loss, and psoriasis. *JAMA Dermatol.* 2013;149:801. https://doi.org/10.1001/jamadermatol.2013.3383
7. Debbaneh M, Millsop JW, Bhatia BK, et al. Diet and psoriasis, part I: Impact of weight loss interventions. *Journal of the American Academy of Dermatology.* 2014;71:133–140. https://doi.org/10.1016/j.jaad.2014.02.012
8. Zuccotti E, Oliveri M, Girometta C, et al. Nutritional strategies for psoriasis: Current scientific evidence in clinical trials. *Eur Rev Med Pharmacol Sci.* 2018;22:8537–8551. https://doi.org/10.26355/eurrev_201812_16554

9. Wu AG, Weinberg JM. The impact of diet on psoriasis. *Cutis.* 2019;104:7–10.
10. de Cabo R, Mattson MP. Effects of intermittent fasting on health, aging, and disease. Longo DL, ed. *N Engl J Med.* 2019;381:2541–2551. https://doi.org/10.1056/NEJMra1905136
11. Mattson MP, Longo VD, Harvie M. Impact of intermittent fasting on health and disease processes. *Ageing Research Reviews.* 2017;39:46–58. https://doi.org/10.1016/j.arr.2016.10.005
12. Anton SD, Moehl K, Donahoo WT, et al. Flipping the metabolic switch: Understanding and applying the health benefits of fasting. *Obesity.* 2018;26:254–268. https://doi.org/10.1002/oby.22065
13. Yang F, Liu C, Liu X, et al. Effect of epidemic intermittent fasting on cardiometabolic risk factors: A systematic review and meta-analysis of randomized controlled trials. *Front Nutr.* 2021;8:669325. https://doi.org/10.3389/fnut.2021.669325
14. Jensen P, Zachariae C, Christensen R, et al. Effect of weight loss on the severity of psoriasis: A randomized clinical study. *JAMA Dermatol.* 2013;149:795. https://doi.org/10.1001/jamadermatol.2013.722
15. Plikus MV, Van Spyk EN, Pham K, et al. The circadian clock in skin: Implications for adult stem cells, tissue regeneration, cancer, aging, and immunity. *J Biol Rhythms.* 2015;30:163–182. https://doi.org/10.1177/0748730414563537
16. Damiani G, Watad A, Bridgewood C, et al. The impact of Ramadan fasting on the reduction of PASI score, in moderate-to-severe psoriatic patients: A real-life multicenter study. *Nutrients.* 2019;11:E277. https://doi.org/10.3390/nu11020277
17. Adawi M, Damiani G, Bragazzi NL, et al. The Impact of intermittent fasting (Ramadan fasting) on psoriatic arthritis disease activity, enthesitis, and dactylitis: A multicentre study. *Nutrients.* 2019;11:E601. https://doi.org/10.3390/nu11030601
18. Macklis P, Adams KM, Li D, et al. The impacts of oral health symptoms, hygiene, and diet on the development and severity of psoriasis. *Dermatol Online J.* 2019;25:13030/qt85z4t7hq. https://doi.org/10.5070/D3257044813
19. Macklis PC, Tyler K, Kaffenberger J, et al. Lifestyle modifications associated with symptom improvement in hidradenitis suppurativa patients. *Arch Dermatol Res.* 2021. https://doi.org/10.1007/s00403-021-02233-y
20. Adawi M, Watad A, Brown S, et al. Ramadan fasting exerts immunomodulatory effects: Insights from a systematic review. *Front Immunol.* 2017;8:1144. https://doi.org/10.3389/fimmu.2017.01144