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EXPLORING THE SYNERGISTIC EFFECTS OF A COMBINED LOW-FODMAP AND GLUTEN-FREE DIET ON SYMPTOM RELIEF AND GUT MICROBIOTA MODULATION IN NON-CELIAC GLUTEN SENSITIVITY: A NOVEL SYSTEMATIC REVIEW AND META-ANALYSIS

Society: AGA**Track:** Microbiome in Gastrointestinal and Liver Diseases**Author(s) and Affiliation(s):**

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Introduction: Non-celiac gluten sensitivity (NCGS) leads to gastrointestinal and non-gastrointestinal symptoms triggered by gluten in individuals without celiac disease or wheat allergy. While its pathophysiology remains unclear, dietary interventions like the low FODMAP diet (LFD) and gluten-free diet (GFD) are used to alleviate symptoms. The LFD, which restricts fermentable oligosaccharides, disaccharides, monosaccharides, and polyols, is commonly used for managing IBS, while the GFD is advised for suspected gluten intolerance. This meta-analysis evaluates the impact of LFD and GFD on symptom severity, gut microbiota, and inflammatory markers in patients with NCGS based on outcomes like the Visual Analogue Scale (VAS) and Irritable Bowel Syndrome Severity Score (IBS-SSS).

Methodology: A systematic search of PubMed, Embase, Cochrane Library, and Web of Science was conducted per PRISMA guidelines to identify randomized controlled trials (RCTs) comparing LFD and GFD in NCGS. Studies were included if they compared the effects of LFD and GFD on symptom severity, gut microbiota, or inflammatory markers and reported outcomes such as VAS or IBS-SSS. Four studies with 350 participants met the inclusion criteria, providing data on symptom severity, microbiota changes, and inflammatory markers. Meta-analyses were conducted using random-effects models to calculate effect sizes for VAS, IBS-SSS, and microbiota outcomes. Statistical significance was set at $p < 0.05$, with pooled mean differences (MDs) and 95% confidence intervals (CIs) presented. Heterogeneity was assessed using Cochran's Q and I^2 statistics. STATA was used for forest plot and metaanalysis.

Results: This meta-analysis included four studies with 350 participants comparing the effects of LFD to standard care or no intervention. The LFD significantly reduced IBS symptom severity, with a pooled MD of 33.9% (95% CI: -33.8%, -34.0%; $p < 0.001$). However, heterogeneity was high (Cochran's Q = 10542.86; $I^2 = 99.97\%$), reflecting variability in study designs and populations. Gut microbiota richness increased significantly by +22% (95% CI: +16% to +28%; $p = 0.002$), measured through 16S rRNA analysis. Adherence to LFD was high, with a retention rate of 75% (95% CI: 68% to 82%), and adverse events were minimal, reported in fewer than 10% of participants.

Conclusion: The low FODMAP diet significantly reduces IBS symptom severity and improves gut microbiota richness compared to standard care or no intervention. Although heterogeneity was high, the diet is effective, well-tolerated, and associated with high adherence and minimal adverse events. These findings support the LFD as a viable option for managing IBS symptoms and enhancing gut health in patients with NCGS. Further research with standardized protocols is needed to confirm these results in diverse populations.

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