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과민성 장증후군에서 제한 식이요법의 효과: 체계적 문헌 고찰과 네트워크 메타분석

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Efficacy of a Restrictive Diet in Irritable Bowel Syndrome: A Systematic Review and Network Meta-analysis

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Background/Aims: Dietary factors can aggravate the symptoms of irritable bowel syndrome (IBS). Many IBS patients try restrictive diets to relieve their symptoms, but the types of diets with an exacerbating factor are unknown. Therefore, this paper reports the results of a systematic review and network meta-analysis of randomized-controlled trials (RCTs) reviewing the efficacy of food restriction diets in IBS.
Methods: The MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, and Clinicaltrials.gov databases were searched until July 21, 2021, to retrieve RCTs assessing the efficacy of restriction diets in adults with IBS. Two independent reviewers performed the eligibility assessment and data abstraction. RCTs that evaluated a restriction diet versus a control diet and assessed the improvement in global IBS symptoms were included. These trials reported a dichotomous assessment of the overall response to therapy.
Results: A total of 1,949 citations were identified. After full-text screening, 14 RCTs were considered eligible for the systematic review and network meta-analysis. A starch- and sucrose-reduced diet and a diet with low-fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) showed significantly better results than a usual diet. Symptom flare-ups in patients on a gluten-free diet were also significantly lower than in those on high-gluten diets.
Conclusions: These findings showed that the starch- and sucrose-reduced, low FODMAP, and gluten-free diets had superior effects in reducing IBS symptoms. Further studies, including head-to-head trials will be needed to establish the effectiveness of dietary restrictions on IBS symptoms. **(Korean J Gastroenterol 2022;80:6-16)**

Key Words: Irritable bowel syndrome; Network meta-analysis; Systematic review; Restrictive diet therapy

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Conflict of interest: None.

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal disorder that affects a high proportion of the population.[1] It is characterized by chronic abdominal pain or discomfort and altered bowel habits without any other structural and biochemical abnormalities.[2] Current medications for IBS target specific mechanisms, such as motility, secretion, or the microbiome. Previous randomized-controlled trials (RCTs) reported that the therapeutic gains offered by these medications are only 8-20% more than that of placebo use, thereby improving the conditions of less than half of the patients.[3]

Owing to the limitations of drug therapy and the long course of IBS, diet appears to play an essential role in managing IBS. Patients with IBS with up to 84% reporting food-related symptoms.[4] Furthermore, another study reported that approximately 50% of patients with IBS have postprandial exacerbations of symptoms within 90 min of eating.[5] The prevalence of perceived food intolerance is very high (70%) with considerable consequences.[6] Therefore, patients with IBS actively follow a restrictive diet, and it is essential to inform them of which foods to restrict.

Various dietary restrictions relieve the symptoms of IBS patients, and these include diets, such as low FODMAP (LFD), gluten-free (GFD), starch- and sucrose-reduced (SSRD), and IgG-exclusion and fasting. Currently, the major focus of a restrictive diet is to reduce the fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs). The absorption of FODMAPs in the small intestine is often inadequate. In such cases, FODMAPs proceed to the large intestine in their undigested forms. This increases the osmotic pressure in the intestinal lumen and gas production by bacterial fermentation. Several studies have suggested that LFD is effective in patients with IBS.[7-9] On the other hand, Moayyedi et al.[10] insisted that only three out of 17 RCTs on the dietary interventions met their eligibility criteria, which was too few to conduct a meta-analysis in the same year. Another major restriction diet is GFD. A previous report hypothesized that a subset of patients with IBS might have gluten intolerance or gluten sensitivity in the absence of celiac disease, and some immune responses to specific food components, such as gluten, may trigger IBS symptoms.[11] Accordingly, several RCT studies were also conducted on GFD to demonstrate its efficacy for IBS patients and reported positive results.[12,13]

Other restrictive diets include SSRD and IgG-exclusion diet. A few RCTs have been conducted for these dietary restrictions and have reported efficacy in relieving the symptoms of patients with IBS.[14,15] Although research shows that generally restrictive diets appear to be effective, it is difficult to demonstrate definitive results because of the difficulties of restrictive diets. In particular, comparison between restrictive diets is more difficult. In this regard, this study conducted a systematic review and network meta-analysis of RCTs to evaluate and compare the efficacy of restrictive diets in patients with IBS.

SUBJECTS AND METHODS

1. Search strategy for article selection

The MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, Clinicaltrials.gov, and Cochrane Database of Systematic Reviews until July 21, 2021, were searched to retrieve RCTs that evaluated the response to food restriction diets in patients with IBS based on some eligibility criteria (Table 1). The search included all languages.

Search terms included the following: “irritable colon”, “irritable bowel syndrome”, “gluten-free”, “gluten-free diet”, “fructose oligosaccharide”, “FODMAP or FODMAPs”, “IgG elimination”, “IgG-exclusion”, “food restriction”, “food restriction diet”, “diet restriction”, “fructan”, “carbohydrate diet”, “sweet”, “sweetener”, “starch free”, “sucrose-free”, “starch reduced”,

Table 1. Eligibility Criteria

- Randomized-controlled trials.
- Adults (aged ≥18 years).
- Diagnosis of IBS based on either meeting popular diagnostic criteria[a] or a physician’s decision.
- Compared GFD, LFD, IgG-exclusion diet, or starch restriction diet with a healthy diet[b], sham diet, usual diet, or high-FODMAP diet.
- All patients were placed on one of four restriction diets, which are GFD, LFD, IgG-exclusion diet, and starch- and sucrose-reduced diet and then randomized to challenge or remain on the diet.
- Duration of dietary intervention and follow-up: ≥7 days.
- Dichotomous assessment identifying the differences in global IBS symptoms or abdominal pain after undergoing a food restriction diet.

IBS, irritable bowel syndrome; GFD, gluten-free diet; LFD, low FODMAP diet; FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.
[a]Rome criteria (I, II, III, or IV), Manning criteria, and Kruis score; [b]The National Institute for Health and Care Excellence (NICE) Guidelines, British Dietetic Association (BDA), traditional diet advice.

Table 2. Characteristics of the 14 Randomized-controlled Trials Included in the Network Meta-analysis

Study	Country	Design	Diet	Participants	Intervention	Methodology	IBS definition	Predominant stool type	Duration of therapy	Outcome
Zhang et al.[7] (2021)	China	Single-center, balanced, randomized (1:1), parallel-group controlled study	Low FODMAP	Adult patients with IBS-D	Low FODMAP versus traditional diet advice	Computer-generated randomization with 1:1 allocation. Patients and investigators were blinded.	Rome III	IBS-D	3 weeks	≥50-point reduction in IBS-SSS between post-intervention and mean baseline scores
Goyal et al.[8] (2021)	India	Prospective, randomized, single-blind trial	Low FODMAP, restrictive (4 weeks) -> modified (16 weeks)	18-65 years-old patients with IBS-D, moderate to severe disease (IBS-SSS >175)	Low FODMAP versus traditional diet advice	Computer-generated randomization in a ratio of 1:1, blinding was not explicitly explained.	Rome IV	IBS-D	4 weeks/ 16 weeks	≥50-point reduction in IBS-SSS between post-intervention and mean baseline scores
Wilson et al.[38] (2020)	UK	Randomized, placebo-controlled, three-arm trial	Low FODMAP	18-65 years-old patients with IBS-D, M, or U	Low FODMAP with placebo versus low FODMAP with B-GOS versus sham diet with placebo	Computerized randomization with 1:1:1 allocation. Patients and investigators were blinded.	Rome III	IBS-D IBS-M IBS-U	4 weeks	IBS-SSS was categorized into mild (75-175) or moderate/severe symptoms (>175)
Nilholm et al.[14] (2019)	Sweden	Randomized, open clinical trial	SSRD	18-70 years-old patients with IBS (IBS-SSS >175)	Starch- and sucrose-reduced diet versus ordinary diet	Randomization method was not explicitly explained. No blinding.	Rome IV	Any type	4 weeks	≥50-point reduction of the total IBS-SSS
McIntosh et al.[23] (2017)	Canada	Prospective, randomized, single-blind parallel study	Low FODMAP	18 years-old or older patients with IBS	Low FODMAP versus high-FODMAP	Computer-generated randomization. The administrator was blinded, but the dietician was not blinded.	Rome III	Any type	3 weeks	≥50-point reduction of the total IBS-SSS
Hustoft et al.[39] (2017)	Norway	Randomized, double-blinded, placebo-controlled, crossover design	Low FODMAP	Patients with IBS-D and M (IBS-SSS >175)	Low FODMAP versus high-FOS diet (high-fructooligosaccharides)	Computer-generated randomization, double-blinded.	Rome III	IBS-D IBS-M	3 weeks +10 days	≥50-point reduction of the total IBS-SSS
Staudacher et al.[40] (2017)	UK	Randomized, placebo-controlled study, 2×2 factorial trial	Low FODMAP	18-65 years-old patients with IBS-D, IBS-M, or IBS-U	Low FODMAP with placebo versus low FODMAP with probiotics versus sham diet with placebo versus sham diet with probiotics	Computerized random allocation, patients and investigators were blinded. The dietician was not blinded.	Rome III	IBS-D IBS-M IBS-U	4 weeks	IBS-SSS, GSRS

Table 2. Continued

Study	Country	Design	Diet	Participants	Intervention	Methodology	IBS definition	Predominant stool type	Duration of therapy	Outcome
Eswaran et al.[41] (2016)	US	Single-center, a randomized-controlled trial	Low FODMAP	Adult patients with IBS-D	Low FODMAP versus modified NICE guidelines	Computer-generated randomization in a 1:1 ratio, dietitians were not blinded, but investigators were blinded.	Rome III	IBS-D	4 weeks	"Adequate relief of overall IBS symptoms" during 50% or more of the last 2 weeks of the study period
Shahbazkhani et al.[12] (2015)	Iran	Double-blinded randomized, placebo-controlled trial	Gluten-free diet	16 years-old or older patients with IBS	Gluten-free diet versus powdered gluten-containing diet	Block randomization method by an independent observer. Both patients and investigators were blinded.	Rome III	Any type	6 weeks/ 6 weeks	VAS
Böhn et al.[9] (2015)	Sweden	Multi-center, parallel, single-blind study	Low FODMAP	18-70 years-old patients with IBS (IBS-SSS >175)	Low FODMAP versus traditional IBS diet	Computer-generated web-based randomization. Patients were blinded.	Rome III	Any type	4 weeks	≥50-point reduction of the total IBS-SSS
Halmos et al.[42] (2014)	Australia	Controlled, crossover study	Low FODMAP	Patients with IBS	Low FODMAP versus typical Australian diet	Computer-generated randomization, blinding was not explicitly explained.	Rome III	Any type	3 weeks	IBS-SSS
Staudacher et al.[43] (2012)	UK	Single-center, randomized-controlled trial	Low FODMAP	18-65 years-old patients with IBS	Low FODMAP versus habitual diet	Computer-generated randomization in a 1:1 ratio, no blinding.	Rome III	Any type	4 weeks	Global symptom question regarding satisfaction
Biesiekierski et al.[13] (2011)	Australia	Double-blinded randomized placebo-controlled trial	Gluten-free diet	16 years-old or older patients with IBS	Gluten-free diet versus gluten-free diet+gluten 16 g/day	Randomized according to a computer-generated list of random numbers. Both patients and investigators were blinded.	Rome III	Any type	6 weeks	"Adequate relief of overall IBS symptoms" during 50% or more of the last 1 week of the study period
Atkinson et al.[15] (2004)	UK	Double-blinded, randomized, controlled, parallel design	Food elimination based on IgG antibodies	18-75 years-old patients with IBS	Elimination diet based on IgG antibodies versus sham diet	Computer-generated randomization.	Rome II	Not specified	12 weeks	IBS-SSS and global impact score

UK, United Kingdom; US, United States; FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols; SSRD, starch- and sucrose-reduced diet; IBS, irritable bowel syndrome; IBS-D, irritable bowel syndrome-diarrhea-dominant type; IBS-M, irritable bowel syndrome-mixed type; IBS-U, irritable bowel syndrome-unsubtyped; IBS-SSS, irritable bowel syndrome-symptom scoring system; GSRS, gastrointestinal symptom rating scale; VAS, visual analog score.

and “sucrose-reduced”, which were combined with AND terms. Additional terms, such as “clinical trials”, “double-blinded”, “blind”, or “randomized-controlled trials”, were also used. Two independent reviewers screened the citations, and a third reviewer resolved the disagreement.

Institutional Review Board approval and written consent were not required for this paper as it was not a systematic investigation involving "human subjects".

2. Eligibility criteria

Two investigators (HS Lee and SJ Yu) performed the eligibility assessment and data extraction based on the eligibility criteria (Table 1). For inclusion, RCTs were reviewed regarding a food restriction diet versus a control diet. The trials included in these analyses reported a dichotomous evaluation of the overall responses to the dietary interventions.

3. Outcome measurements

The primary outcome was an improved global response in IBS symptoms or abdominal pain. The strictest outcome that minimized the placebo response rate was used if definitions of reduced symptoms differed within the same study. For example, an IBS symptom improvement rate of >40% would be selected instead of an improvement rate of >20%.

4. Data extraction

Two independent researchers (HS Lee and SJ Yu) performed data collection. Table 2 lists the characteristics of the final 14 RCTs selected. Data included the name of the first author, publication year, country of publication, inclusion criteria, primary endpoint, type of restriction diet, type of the control group, number of patients, age, duration of restriction diet, and outcome measurements. Data were extracted by an intention-to-treat analysis, with dropouts considered treatment failures. Disagreements were resolved by a third reviewer (HB Lee).

5. Evaluation for the risk of bias and grading of recommendations, assessment, development, and evaluation methodology

Two investigators performed a risk of bias assessment using RoB2.0 (2016). All the studies were evaluated based on reports of blinding, allocation, randomization, and outcome measurements (Table 3). Grading of the evidence was conducted according to the Grading of Recommendations, Assessment, Development, and Evaluation methodology using GRADEPro GDT.

6. Data synthesis and network meta-analysis

Network meta-analysis was conducted using the frequentist model, and the netmeta statistical program package (version 0.9-0) was used. The R program (version 3.4.2; https://cran.rproject.org/web/packages/netmeta/index.html) was also used. This report was written according to the Preferred

Table 3. Risk of Bias of the 14 Randomized-controlled Trials Included in the Network Meta-analysis

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Overall quality
Zhang et al.[7] (2021)	Low	Low	Low	Low	Low	Low	Good
Goyal et al.[8] (2021)	Low	Low	High	Low	Low	Low	Good
Wilson et al.[38] (2020)	Low	Low	Unclear	Unclear	Low	Low	Good
Nilholm et al.[14] (2019)	Unclear	Unclear	High	High	Low	Low	Weak
McIntosh et al.[23] (2017)	Low	Low	Unclear	Unclear	Low	Low	Good
Hustoft et al.[39] (2017)	Low	Low	Low	Unclear	Low	Low	Good
Staudacher et al.[40] (2017)	Low	Low	Low	Low	Low	Low	Good
Eswaran et al.[41] (2016)	Low	Unclear	Unclear	Low	Low	Low	Good
Shahbazkhani et al.[12] (2015)	Low	Low	Low	Low	Low	Low	Good
Böhn et al.[9] (2015)	Low	Low	Low	High	Low	Low	Good
Halmos et al.[42] (2014)	Low	Unclear	Low	Unclear	Low	Low	Good
Staudacher et al.[43] (2012)	Low	Low	Unclear	Unclear	Low	Low	Good
Biesiekierski et al.[13] (2011)	Low	Low	Low	Unclear	Low	Low	Good
Atkinson et al.[15] (2004)	Low	Low	Low	Low	Low	Low	Good

Reporting Items for Systematic Reviews and Meta-Analyses guidelines for network meta-analyses[16] and the efficacy of each dietary intervention was compared directly and indirectly. The network meta-analyses would help rank the order of the treatment options, thereby informing medical decisions.[17]

This study examined the network of evidence by making a network plot with the thickness size of the connection in proportion to the number of studies. The collective OR with 95% CIs was determined to express the effects of each dietary intervention using a fixed-effect model. The OR was used for failure to achieve a global IBS symptom response. The dietary intervention showed significant efficacy over a sham diet if the 95% CI does not include 1 and the OR is <1.

The statistical heterogeneity among all the studies was tested using the I^2 measure on the netmeta statistical package. The heterogeneity is considered low when I^2 <50%. However, I^2 ≥75% indicated a relatively high level of heterogeneity.[18] The literature search retrieved 3,460 citations, of which 666 were obtained on MEDLINE, 2,146 on EMBASE, and 648 on the Cochrane Central Register of Controlled Trials. Thirty-three full-text articles were reviewed for eligibility, and 19 articles were excluded. A final total of 14 eligible studies were identified for a systematic review and network meta-analysis of RCTs (Fig. 1).

RESULTS

Fig. 2 presents the network of evidence of various dietary restriction studies. The thickness of each line between the two studies indicates the number of studies to which the two dietary restrictions were compared; a thicker line indicates that there were more results. For example, comparative studies between LFD and a healthy diet were conducted the most. Following this, more comparative studies were conducted in the order of sham diet, usual diet, and high FODMAP (HFD). For the IgG-exclusion diet, only a comparative study with the sham diet was performed, and a comparative study with the usual diet was performed for SSRD. Considering the thickness of the lines of the IgG-exclusion diet with the sham diet and

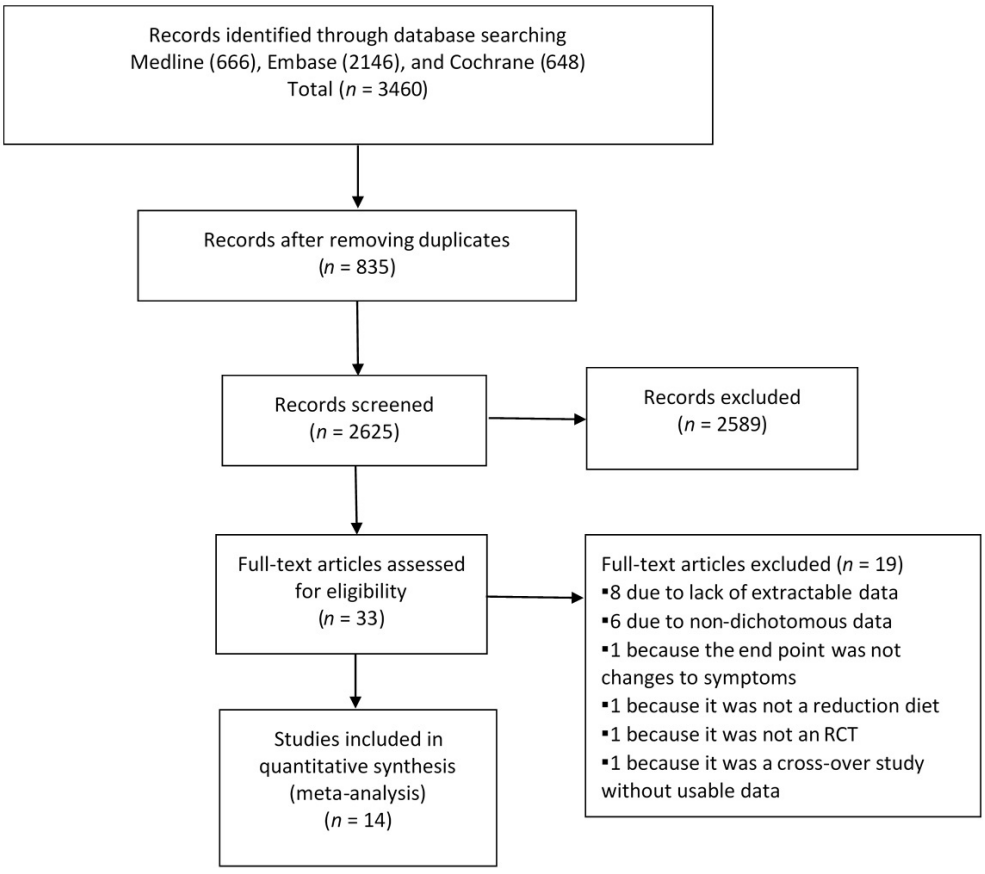

Fig. 1. Flow diagram of the selection of articles for inclusion in the meta-analysis.

the SSRD with the usual diet, the network of evidence is not very strong. There is no comparative study of IgG-exclusion diet with LFD and SSRD with LFD, but the relative effects can be compared by supposing a sham diet and usual diet as mediators.

Fig. 3 shows the network of evidence for GFD and high gluten diet (HGD). Only studies comparing a GFD with a HGD were found, and there were no dietary studies that could serve as mediators, such as a usual or sham diet. As a result, network evidence is expressed as one separate line.

Fig. 4 presents the relative difference in OR of the various restriction diets. In this plot, the standard was the usual diet, and the OR of SSRD (0.16), LFD (0.24), healthy diet (0.37), IgG-exclusion diet (0.37), and sham diet (0.60) was <1. Among them, the OR of the SSRD and LFD was statistically significant. The HFD (1.51) exhibited an OR >1 compared to the usual diet.

Fig. 5 shows the OR of the GFD (0.09) compared to the HGD, which was statistically significant. Table 2 lists the characteristics of all studies included in this network meta-analysis. It included 10 LFD studies, one SSRD study, one IgG-exclusion diet study, and two GFD studies. LFD is the most actively studied, with 10 studies. Of the 10 LFD studies, four studies were compared with a healthy diet, two studies were the usual diet, two studies were sham diet, and two studies were compared with HFD. An SSRD study was compared with a usual diet, and an IgG-exclusion diet study was compared with a sham diet. Both GFD studies were compared with a HGD.

DISCUSSION

Several key observations were made through a systematic review and network meta-analysis. First, SSRD and LFD are more effective in reducing IBS symptoms compared to a usual diet. Second, GFD is more effective in reducing the IBS symptoms than HGD. Third, an IgG-exclusion diet and a healthy diet did not prove to be significantly more effective than a usual diet.

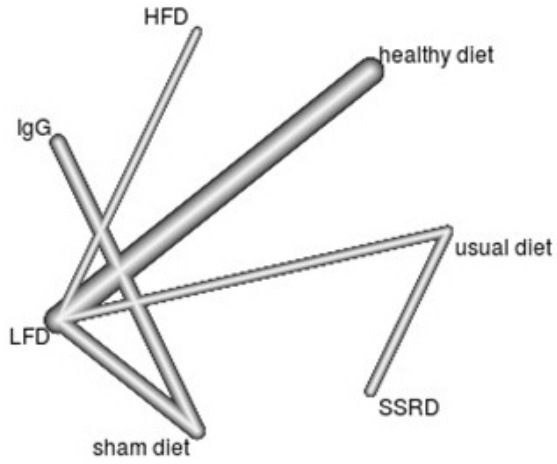

Fig. 2. Network of evidence for food restriction diet in patients with IBS except for GFD. LFD, low-FODMAP diet; IgG, IgG-exclusion diet; HFD, high-FODMAP diet; SSRD, starch-, and sucrose-reduced diet; IBS, irritable bowel syndrome; GFD, gluten-free diet; FODMAPs, fermentable oligosaccharides, disaccharides, monosaccharides, and polyols.

Fig. 3. Network of evidence for a gluten-free diet in patients with IBS. GFD, gluten-free diet; HGD, high-gluten diet; IBS, irritable bowel syndrome.

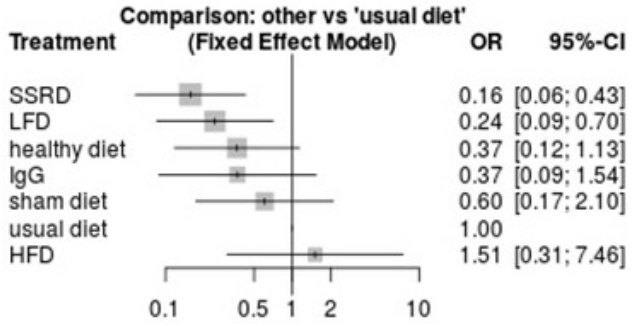

Fig. 4. Forest plot of the indirect evidence for the failure to achieve a global IBS symptom response to food restriction diets except for GFD. SSRD, starch-, and sucrose-reduced diet; LFD, low-FODMAP diet; IgG, immunoglobulin G; HFD, high-FODMAP diet; OR, odds ratio; CI, confidence interval; IBS, irritable bowel syndrome; GFD, gluten-free diet; FODMAP, fermentable oligosaccharides, disaccharides, monosaccharides, and polyol.

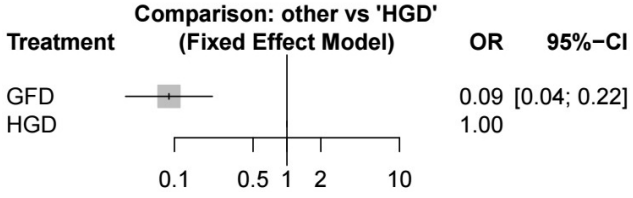

Fig. 5. Forest plot of the indirect evidence for the failure to achieve a global IBS symptom response to GFD. GFD, gluten-free diet; HGD, high gluten diet; OR, odds ratio; CI, confidence interval; IBS, irritable bowel syndrome; GFD, gluten-free diet.

SSRD was introduced as a dietary intervention for IBS in clinical research after discovering the increased prevalence of rare pathogenic *SI* variants in IBS.[19] The first clinical trial by Nilholm et al.[20] described the significant differences in GI symptoms and psychological well-being between the intervention group on SSRD and the control group after 2 weeks of treatment. The second clinical trial by Nilholm et al.[14] showed decreased changes in total IBS-SSS and extra-intestinal IBS-SSS scores in the intervention group on SSRD compared to the control group ($p<0.001$ for all). In this study, SSRD showed the smallest OR (OR, 0.16; [95% CI, 0.06; 0.43]) compared to other restriction diets. On the other hand, additional RCTs should be conducted for an accurate comparison because only one RCT of SSRD was included in this meta-analysis.

Unabsorbed carbohydrates in the colon, such as fructans and galactooligosaccharides, are fermented by bacteria, giving rise to gas production. Subsequent luminal distension leads to functional GI symptoms, such as abdominal pain and bloating in patients with IBS.[21] One study showed that a high-FODMAP diet induced a marked increase in the 14-hour breath hydrogen production after 2 weeks compared to an LFD in 15 patients with IBS and 15 healthy individuals.[22] An RCT in 2017 showed that an LFD for 3 weeks reduced the 5-hour breath hydrogen following a lactulose challenge compared with a high-FODMAP diet.[23] The two studies suggest that an LFD may lead to a beneficial shift in colonic fermentation patterns, which is a feasible dietary intervention for patients with IBS. In this study, LFD had the second lowest OR (OR, 0.24; [95% CI, 0.09; 0.70]). Recently, LFD was considered the most effective dietary restriction, and research on LFD is being actively conducted. In 2015, with the accumulation of research results on the effects of LFD, the National Institute for Health and Care Excellence (NICE) newly added guidelines for trying a restrictive diet, especially LFD, when a person's IBS symptoms persist while following general dietary advice.[24] Another meta-analysis that did not include SSRD showed that LFD ranked first in efficacy across all the endpoints studied compared to other interventions, including the NICE and British Dietetic Association (BDA) dietary recommendations for patients with IBS.[25] Furthermore, on the long-term follow-up, no difference was found in the total energy intake and macronutrient and micronutrient intake between individuals on the personalization phase of the LFD and those on a habitual diet.[26] On the other hand, LFD is restrictive and not easy to adopt and follow. LFD has three stages (the substitution of foods with low FODMAP choices, a gradual reintroduction of foods into the diet while assessing symptoms, and personalization of the diet to avoid foods that trigger symptoms). The healthcare provider needs to direct the patients through the stages. This complexity and the associated potential for malnutrition make LFD difficult to adopt.[27]

Gluten intolerance in people without celiac disease is common and has recently been described as non-celiac gluten sensitivity.[28] The GI symptoms and signs in many patients with IBS appear to improve after adopting a GFD. A double-blinded RCT in 2015 evaluated patients with IBS presenting with GI and extra-GI symptoms. They revealed significant differences between a gluten-containing diet and a control diet regarding symptom control.[12] A GFD is less restrictive and easier to implement in everyday life and can be suggested for patients who recognize gluten as a trigger of symptoms. GFD was found to be significantly effective in this study compared to HFD. Unfortunately, there was no RCT comparing a GFD to the usual diet, so GFD could not be subjected to network meta-analysis with other restrictive diets (LFD and SSRD). Although no study directly compared GFD with LFD, a review paper on this topic was published in 2020.[29] Several papers reported that an LFD is more effective in IBS than a GFD,[30-32] but a GFD is easier to apply in real life. Thus, an LFD may be feasible if a GFD is applied and the symptoms of IBS do not improve.

Some clinical research about IgG-exclusion diets has been conducted since the first study by Atkinson et al.[15] in 2004. Guo et al.[33] implemented a 12-week specific food exclusion diet after obtaining increased titers of specific IgG antibodies against 14 common food antigens. The diet resulted in significant symptomatic improvements in abdominal pain, diarrhea frequency, abdominal distension, general feelings of distress, and the total symptom score compared with the baseline in patients with IBS-D. Aydinlar et al.[34] reported that IBS symptoms, such as pain and bloating, and migraine symptoms, may improve by eliminating IgG after IgG antibody tests against 270 food allergens. Nevertheless, the IBS symptom response of the IgG-exclusion diet in this network meta-analysis was not significantly lower than that of the usual diet (OR, 0.37; [95% CI, 0.09; 1.54]). Currently, food restriction using the IgG4 test is used commercially, but the evidence is

insufficient. Additional RCTs will be needed to confirm the efficacy of the IgG-exclusion diet.

In this study, the healthy diet tended to be more effective in improving IBS symptoms than the usual diet, but it was not statistically significant. A healthy diet is a term that includes traditional diet advice, the NICE/BDA guidelines, and modified NICE guidelines. Traditional diet advice was used in the three RCTs,[7-9] and the definitions used in the three papers were similar. Traditional diet advice is to reduce intake of fatty or spicy foods, coffee, and alcohol, eat three regular meals a day, and not eat too much or too little.[7] This concept is based on the BDA/NICE guidelines.[35,36] The NICE guidelines outline dietary and nutritional advice for patients with IBS in the United Kingdom. They were introduced in 2008 and modified in 2017. Under the standardized instructions of the guidelines, the NICE group was educated to eat small-volume meals frequently, avoid missing meals or long intervals between eating, avoid trigger foods, and avoid excess alcohol and caffeine. The BDA guidelines for IBS provide evidence statements, recommendations, and practical considerations for dietitians. It recommends eliminating milk and dairy products, avoiding wheat bran, recommending ground linseed for IBS-C, reducing the intake of fermentable carbohydrates, considering using probiotics after reducing fermentable carbohydrates, and considering an empirical elimination diet.[35] One study reported that 3%, 11%, and 86% of patients with IBS preferred the LFD, GFD, and balanced diet, respectively.[30] A healthy diet, as in a balanced diet, is easier to follow than any other restriction diet.

This systematic review and network analysis had some limitations. First, the GFD was not included in the network meta-analysis because there were no studies comparing GFD with other restrictive diets. Additional RCTs that compare a GFD to an LFD or usual diet will be needed in the future. Second, insufficient information was obtained to determine if an IgG-exclusion diet and SSRD are truly effective in improving IBS symptoms, considering that only one RCT of the IgG-exclusion diet and just one RCT of SSRD were included in this network meta-analysis. Third, the main issue for researchers evaluating restrictive diets in IBS is the diet to implement in the control group. What to use as a control diet among usual, sham, or healthy diets is a key challenge for researchers.[37] Overall, network meta-analysis involves a complex network of factors and should be interpreted carefully.

Dietary treatment for IBS is still insufficient, but it is trying to establish itself as one of the treatment methods through various trials and diversification of dietary methods. In particular, dietary treatment methods, such as SSRD, LFD, and GFD, are the most advanced and could be established as the significant restrictive dietary interventions in the near future. As the pathophysiology of IBS is gradually being elucidated, it is hoped that new methods for the dietary treatment of IBS can be developed.

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