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The low-FODMAP diet as a dietary intervention in Irritable Bowel Syndrome: a literature review

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Declaro para os devidos efeitos ter atuado com integridade na elaboração deste Trabalho de Projeto, atesto a originalidade do trabalho, confirmo que não incorri em plágio e que todas as frases que retirei de textos de outros autores foram devidamente citadas ou redigidas com outras palavras e devidamente referenciadas na bibliografia

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(Ana Margarida Pereira Azevedo)

Trabalho apresentado à Universidade Fernando Pessoa como parte dos requisitos para obtenção do grau de licenciado em Ciências da Nutrição

Orientadora:

Professora Doutora Ana Sofia Sousa

Coorientadora:

Professora Doutora Catarina Simões

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I. Index

II. Figures and Tables Index

III. Abbreviation's list

BSC – Bristol stool scale

DRI`s – Dietary Reference Intake

FODMAPs - Fermentable Oligo-, Di-, and Monosaccharides and Polyols

FOS – Fructo-oligosaccharides

GI - Gastrointestinal

GOS- Galacto-oligosaccharides

HFD – High-FODMAP diet

IBD – Inflammatory Bowel Disease

IBS – Irritable Bowel Syndrome

IBS-C – IBS Constipation predominant

IBS-D – IBS Diarrhoea predominant

IBS-M – IBS Mixed-type

IBS-SSS score – IBS symptom severity scoring system

LFD – Low-FODMAP Diet

LLD – Low-lactose diet

NICE – National Institute for Health and Care Excellence

Qol – Quality of life

RCT – Randomized controlled Trial

rRNA – Ribonucleic Acid

SCFA – Short – chain fatty acids

VAS – Symptom Severity Score

The low-FODMAP diet as a dietary intervention in Irritable Bowel Syndrome: a literature review

Dieta pobre em FODMAP como uma intervenção dietética na Síndrome do intestino irritável: Revisão da Literatura

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V. Abstract

The Irritable Bowel Syndrome (IBS) is a multifactorial and remitting disease characterized by the onset of various symptoms such as abdominal pain, discomfort, bloating, flatulence and altered bowel habits (diarrhoea, constipation or both) and where diet is considered, by the IBS patients, the trigger for the symptoms.

There are several therapies for the treatment of this condition such as: pharmacological treatments, dietary interventions and alternative treatments. However, dietary intervention is the most common therapy used because it is shown that it has benefits in the improvement of the IBS symptoms. Several approaches to this end have been studied over the years. Among this approaches the low-FODMAP diet (LFD) has been created specifically for these patients and several studies evidence its success.

This literature review aims to review the current evidence achieved until now on implementation, benefits and limitations of LFD in IBS.

This study was performed by the search in the online databases PubMed and Science Direct.

To conclude, this literature review shows several benefits on the implementation of LFD in IBS patients, a positive change on disease course as well as a better quality of life. Nevertheless, this implementation can lead to adverse effects such as malnutrition and the impact on composition of the intestinal microbiota. Although this diet can be used in clinical practice for the management of IBS, individualization and supervision by a trained nutritionist is necessary in order to avoid negative consequences such as malnutrition.

Nevertheless, more studies on long-term effects are necessary especially regarding the impact on gut microbiota.

Keywords: Irritable Bowel Syndrome, Fermentable Oligo-, Di-, and Monosaccharides and Polyols (FODMAPs), Low-FODMAP diet

VI. Resumo

A Síndrome do Intestino Irritável (SII) é uma doença multifatorial e remitente caracterizada pelo aparecimento de vários sintomas, como dor, desconforto abdominal, distensão abdominal, flatulência e hábitos intestinais alterados (diarreia, obstipação ou ambos) e a dieta é considerada, pelos pacientes, o estímulo para os sintomas.

Existem várias terapias para o tratamento desta condição, tais como: tratamento farmacológico, intervenção dietética e tratamentos alternativos. No entanto, a intervenção dietética é a terapia mais usada porque demonstrou ser benéfica na melhoria dos sintomas da SII. Várias abordagens para esse fim foram estudadas ao longo dos anos. Dentre essas abordagens, a dieta pobre em FODMAPs foi criada especificamente para esses pacientes e vários estudos evidenciam o seu sucesso.

Esta revisão da literatura tem como objetivo rever toda a evidência alcançada até agora na implementação, benefícios e limitações sobre a dieta pobre em FODMAP na SII.

Este estudo foi feito por meio de pesquisa em bases de dados online a PubMed e a Science Direct.

Para concluir, esta revisão da literatura mostra vários benefícios na implementação da LFD em pacientes com SII, uma mudança positiva no curso da doença, bem como uma melhoria na qualidade de vida. No entanto, essa implementação também gerou efeitos adversos como a desnutrição e o impacto na composição da microbiota intestinal. Apesar desta dieta poder ser usada na prática clínica para o controlo da SII, é necessária a individualização e supervisão de um nutricionista treinado no sentido de evitar consequências negativas como a desnutrição.

No entanto, mais estudos acerca dos efeitos a longo prazo são necessários principalmente no que diz respeito ao impacto na microbiota intestinal.

Palavras-chave: Síndrome do Intestino Irritável, FODMAPs, Dieta Pobre em FODMAPs

1. Introduction

The Irritable Bowel Syndrome (IBS) is a chronic disorder that compromises gastrointestinal (GI) function. This syndrome is characterized by symptoms such as abdominal pain, discomfort, bloating, flatulence and altered bowel habits (diarrhoea, constipation or both) (1–4).

IBS is one of the most common GI disorders and the prevalence of this condition differs across the world, showing a global prevalence of circa 8% (4). This syndrome is more prevalent among women and young adults, aged between 20 and 30 years, and rarely manifests after 50 years old (1,2,4,5). In Western countries, where this condition is more often diagnosed, was observed that these patients present a high rate of impact on their Quality of Life (Qol) (4,6). In fact, IBS is one of the most debilitating diseases due to the impact in the GI tract in comparison with other chronic diseases such as diabetes and gastroesophageal reflux disease (GERD) (6).

The prevalence of IBS has been increasing. IBS pathophysiology is complex and multifactorial and not fully understood yet (7). Nevertheless, some hypotheses have been proposed: dysbiosis, i.e. an imbalance of the normal intestinal microbiota, abnormal gut motility, inflammation, psychological distress, increased mucosal permeability, impaired immune function, visceral hypersensitivity and genetic factors (7).

Psychological factors such as traumatic life experiences (psychological and physical abuse) play an important role in the development of this chronic disease once these experiences instigate hypothalamic-pituitary axis hormones as well as neurotransmitters that may cause a dysregulation of the signalling between the central and enteric nervous system which leads to gut dysfunction (4).

IBS present a higher predisposition for dysbiosis of the gut microbiota demonstrating a higher proportion of pathogenic bacteria and decreased of the beneficial bacteria (8). These patients show a reduction in numbers and diversity of Bifidobacteria and Lactobacilli compared with healthy people (6,9). This reduction exerts adverse effects because these bacteria are important for the production of short-chain fatty acids (SCFAs), barrier defense, gut hormone regulation, immunomodulation. So, this dysbiosis can cause a dysregulation of the normal GI function and lead to IBS (9).

Additionally, a proportion of patients with IBS is known to have excessive bacterial growth on the small intestine (4). Circa 25% IBS patients have an initial event that is characterized by an enteric infection that causes the disease. This group of patients is denominated postinfectious IBS (PI-IBS). This phenomenon happens due to the fact that symptoms of abdominal discomfort, bloating and diarrhoea persists even after infection is treated (4).

Nevertheless, food is considered to be the most outstanding cause of IBS symptoms. There are several mechanisms that can lead to this condition including the fermentation of short-chain carbohydrates by enteric bacteria, food allergy, food sensitivity, alterations in gut motility, luminal fluid shifts highly osmotic dietary substances, changes in gut hormones and alterations in gut microbiome (4). IBS patients present a high prevalence of food sensitivity and intolerance when compared to general population. Two-thirds of IBS patients have at least one food intolerance (4,10). For that reason, in the majority of studies, most patients mention that food is the common trigger for the symptoms and many dietary components like high-carbohydrate foods, fat, beans, lentils, foods reach in spice, dairy, coffee or alcohol may induce GI symptoms and so they tend to avoid some foods (1–3,7,11,12). Circa 60% of patients report that IBS symptoms aggravates after the ingestion of food (4).

The diagnosis of IBS is highly difficult since this syndrome is a remitting condition with symptom changes over the time. Moreover, IBS symptoms are similar to the symptoms of several other disorders and there is not a biomarker for this syndrome. Therefore, IBS diagnosis can be subjective (7,13).

As IBS is a very debilitating disease associated with a high healthcare cost, it is important to treat or minimize the consequences. Thus, a wide range of treatment strategies, both non-pharmacological and pharmacological, have been implemented in clinical practice (14).

The pharmacological treatment is implemented with the only goal of alleviate the symptoms in the patients. Thus, there are a wide variety of drugs that can ameliorate them such as: laxatives for constipation, antispasmodics for abdominal pain and anti-motility drugs for diarrhoea. This approach can be used before or after the implementation of lifestyle and dietary interventions (14). However, they are not all helpful and effective (12).

The non-pharmacological treatments comprehend alternative interventions, psychological therapies and lifestyle and dietary interventions.

Since a high proportion of patients reports that food is a major trigger for IBS symptoms and dietary restrictions demonstrate to improve the symptoms, nutrition intervention is a frequent option (12). Through the last decades, several dietary interventions have been studied and applied on IBS. Among those interventions are the Gluten-Free Diet, the Low Fructose/Fructan Diet, the Lactose-free diet, the Immunoglobulin – G (Ig-G) based avoidance diet, the Very-low carbohydrate diet or Ketogenic Diet, Fibre supplementation, Low-fat Diet, NICE guidelines and the Low-FODMAP Diet (LFD).

The Gluten-Free Diet is characterized by the elimination of gluten from the diet (16). Gluten is a complex of high molecular-weight proteins that are made of glutenin and gliadin and are present in wheat, rye and barley (17,18). In fact, wheat-containing foods are widely consumed around the world and are responsible for the intake of more than 50% of the daily energy, although their consumption has been decreasing. Wheat is constituted by proteins (gluten and albumins) and carbohydrates (starch that contains fructans) (17). This diet was firstly used for celiac disease (17). However, the effect on the reduction of GI symptoms in IBS patients has been widely studied (19,20). Notwithstanding this, several studies have reported heterogeneous results. Thus, the use of this diet as an intervention in IBS needs further studies (19,20).

Low Fructose/Fructan Diet is a diet characterized by the avoidance of foods high in fructose and fructans (16). Fructan is an oligosaccharide, is consider a FODMAP (Fermentable Oligo-, Di-, and Monosaccharides and Polyols) and have been proved that the ingestion of fructan sources can worsen IBS (21). There are several studies reporting the efficacy of this diet on IBS symptoms, especially among patients who present fructose malabsorption (16,22).

Lactose-free diet consists of lactose elimination (16). Lactose is a disaccharide composed by glucose and galactose (17,23). This carbohydrate is considered a FODMAP only if it is not digested in the gut by lactase (17). It is known that only 25% to 33% individuals maintain the capacity to digest lactose in adulthood (17). In lactose intolerance, lactose reaches the colon and is fermented by microbiota. This formation causes several GI symptoms such as, flatulence, bloating, abdominal pain and diarrhoea

(17). For several years researchers believed that lactose intolerance was the cause of IBS. However, this theory was later rejected and was proven that these are two different conditions with different aetiology and pathophysiology. In fact, there are IBS patients that are lactose intolerant and IBS patients that present normal lactose digestion (17). Thus, this diet is only an option for IBS patients with lactose intolerance (17).

Very-low carbohydrate diet is characterized by the intake of only 20g of carbohydrates per day, nearly 5% of daily energetic intake (16). This diet has been recommended for weight loss, diabetes, control of metabolic disease and exercise performance (17) . However, for IBS patients only one study has been performed and reported a benefit on the adequate relief of the symptoms (abdominal pain, stool consistency/frequency, and Qol) in 77% IBS-D patients. This improvement is due to the fact that there is a reduction of carbohydrates which is a macronutrient that can induce GI symptoms in patients with IBS. However, there are not sufficient studies to support the implementation of this diet in IBS patients (16,17,25).

Low-fat Diet is characterized by the implementation of a diet with fewer than 27g of fat (16). This approach was only evaluated through observational studies and noncontrolled trials and, in fact, a diet high in fat induces the inhibition of the GI motility and the release of gas which causes the IBS symptoms. The studies report an improvement in the IBS symptoms, specifically abdominal pain. However, there are not randomized controlled trials to support the application of the diet in IBS patients (16,26).

Ig-G based avoidance diet was proposed for IBS patients as an alternative for the very restrictive diets (lactose-free diet, very-low carbohydrate diet) (17). This diet results from the analysis on the amount of Ig-G produced when consuming the components of food such as egg, crab, shrimp, soybean, and wheat. Then, the exclusion of the foods that increase the levels of Ig-G is performed (17). However, evidence is scarce regarding the application of this diet in IBS patients (17,24).

Fibre supplementation is a diet that for many years was used in IBS patients (12). A Dietary fibre is a carbohydrate that is not digestible in the small intestine and its present in cereals, fruits and vegetables (17). These components can be divided in two groups: soluble and insoluble (17). A widely number of studies show benefits in the implementation of this diet on the improvement in all IBS patients, particularly in IBS-C patients (17,27). However, this improvement is only viewed in studies that used soluble

fibres because the only problem triggered is the formation of gas that induce the GI symptoms and is more prominent in the insoluble fibres (17,27).

The National Institute for Health and Care Excellence (NICE) Guidelines from United Kingdom were the first recommendations established for IBS patients in primary care setting (28). These guidelines present a set of steps to diagnose this syndrome and provides information to the patients that are diagnosed (28). This information includes incentive to lifestyle changes: healthy eating habits, increase physical activity, follow simple dietary advice (regular eating patterns, completely chewing meals, avoiding missing meals and adequate fluid ingestion), avoid the specific foods that trigger the IBS symptoms such as caffeine, alcohol, spicy and fatty foods and limit the ingestion of resistant starch and restrict gas-producing food items (onions, cabbage, beans, carbonated beverages and artificial sweeteners) (28). These guidelines are implemented on primary care in IBS patients and were developed based in systematic reviews. However, if these initial strategies are not efficient in the improvement of the IBS symptoms, it is necessary to consider another approach (28).

The Low-FODMAP Diet (LFD) is the most studied and the most commonly diet used in IBS patients (16). This diet has been proposed in the Monash University in Australia by Peter Gibson and Susan Shepherd (16). Prospective studies reported a benefit in the improvement on 75% of IBS patients in GI and non-GI symptoms and also in Qol (1–3,5,16). This improvement is due to the reduction in fermentable carbohydrates that contributes to the reduction of the production of gas and consequently the abdominal distension (7).

Although LFD is a promising approach for IBS management in clinical practice, this diet presents some limitations: this is a complex diet, may lead to nutritional deficits, needs monitorization and individualization and has impact on gut microbiota.

The present study aims to review the current evidence on the implementation, benefits and limitations of LFD in IBS treatment and management.

2. Methodology

This review article was performed through the information obtained by search in the bibliographical databases, PubMed and Science Direct.

This search was conducted by the introduction of the following search terms: “low FODMAP diet” AND “irritable bowel syndrome” AND “Oligosaccharides” AND “Disaccharides” AND “Monosaccharides” AND “Polyols”.

In the first search, on PubMed, 56 results were obtained and in the second search, on Science Direct, 195 results were obtained. Then, these studies were selected according to the relevance of the study through the implementation of the inclusion and exclusion criteria. The inclusion criteria were clinical trials, observational studies and articles that were conducted in humans. The exclusion criteria were letters, comments, reviews, meta-analyses, animal studies, article language was not in English and non-association of LFD with IBS. After analysing all the articles, 30 articles were excluded from PubMed and 193 from Science Direct.

The additional bibliographic references were obtained through a snowball research to obtain even more relevant articles. 54 articles were selected. The flow diagram (**Figure 1**) describes the search terms used and the final articles selected for this review.

3. FODMAPS

FODMAP is the acronym for “Fermentable Oligo-, Di-, and Monosaccharides and Polyols” and are a group of short-chain carbohydrates that are poorly digested and absorbed in the small intestine and therefore are fermented by intestinal microbiota in the large intestine producing SCFA and gases. The excessive production of these components can improve the osmotic effects causing water retention and luminal distension and consequently the GI symptoms (2,3). These carbohydrates include fructose, lactose, polyols, fructans, and galacto-oligosaccharides (GOS) (3), which are present in various of our daily routine diet including simple sugars, fruits, vegetables and cereals (29) .

Oligosaccharides are fructans and GOS. These carbohydrates cannot be digested in the small intestine because the humans do not have enzymes to break their bonds (6). Fructans are the major source of fermentable carbohydrates and are described by being polymers of fructose molecules that can be linear or branched and the human GI tract does not have the enzyme to digest the β-(2-1) fructosyl-fructose glycosidic bond (6). They are widely found in plants and play the role of storage carbohydrates and in our diet, they are most achieved from onions and wheat not because of their highest content but because they are consumed in large amounts (6). GOS are characterized by the presence of galactose monomers with a terminal glucose unit and the human GI tract does not have

an α-galactosidase enzyme. They are present in our diet on human milk, pulses, legumes and in certain nuts, grains and seeds (6).

The lactose, an example of a **Disaccharide**, is composed by glucose and galactose, and these carbohydrates, in few people, are incompletely digested and absorbed because they are hydrolysed by the lactase enzyme and their production is deficient or in low level (hypolactasia) on up 70% of humans (6). In case of IBS patients, it is observed in 18-82% and just is consider a FODMAP if the patient has this condition. The lactose that is not absorbed reach the large intestine where it is fermented by the intestinal microbiota. In our diet, we can find them on milk, ice cream, cheese, bread, cakes, yogurt (6).

Monosaccharides as fructose is a simple sugar that is characterized by presenting 6-carbons and they do not need to be digested. So, they have transporters to facilitate the absorption, Glucose Transporter type 5 that are fructose specific or Glucose Transporter type 2 on the apical membrane of the intestinal epithelium (6). However, they are dose-dependently and variably absorbed. Some studies highlight that a consumption of 35g of fructose alone is incompletely absorbed by 30-60% of the population. Fructose is considered a FODMAP only if it is not absorbed and reach the colon. Dietary sources of fructose are fruit, fruit products and products sweetened with high-fructose sweeteners (6).

Polyols such as sorbitol, mannitol, xylitol and maltitol are sugar alcohols and its absorption is variable among the general population and influenced by molecular weight and organic diseases (6). Studies demonstrated that sorbitol is not absorbed by 60-70% of healthy people and individuals with IBS have an incomplete absorption on a 10g/dose. (6). The sources of polyols are fruits, vegetables and chewing gum (6).

3.1. The FODMAP hypothesis for IBS patients

It has been demonstrated that the intake of FODMAPs may trigger IBS symptoms (26,30). In fact, there are a number of carbohydrates that are poorly digested in the GI tract and when these compounds reach large intestine they are fermented by gut microbiota (30). This fermentation provides the formation of short-chain fatty acids (SCFAs) and induce hydrogen and methane production in the gut (16). The change in the pH levels and the possible alteration in the gut microbiota may lead to alterations in colonic function and local inflammation (16). Also, these carbohydrates are small

molecules with high osmotic activity which leads to the accumulation of water in the colon. A scheme of a set of high-FODMAP food sources is presented in **Figure 2**.

3.2. Low- FODMAP diet

LFD is now commonly used in the management of IBS (11). In the implementation of this diet, it is recommended the exclusion of all foods rich in FODMAPs with the intention of limiting the presence of substances that are widely fermented by the intestinal microbiota and that are osmotically active. The propose of this exclusion is minimize the production of gas and consequently luminal distention and try to improve the symptoms (7,31). When symptom relief is achieved patients reintroduce some of the high-FODMAP foods individually to test for tolerance with the goal of achieving long-term symptoms control (16).

LFD is a restrictive diet with a complex intervention that can lead to nutritional deficits. There may be an inadequate intake of carbohydrates, energy, vitamin B, iron, calcium and fibre that can compromise the health of patients because the intake of foods rich in that components are restricted (i.e., milk, fruits, vegetables, cereals). So, this diet must be always implemented with the advice and supervision of a trained professional (32).

A large amount of data highlight that LFD was successful in 50-80% of patients with IBS in comparison to a regular diet or a commonly recommended diet. A reduction of the IBS symptom severity scoring system (IBS-SSS), i.e., a tool used on IBS patients to access the severity of the disease, is commonly achieved. This tool also includes questions related to the intensity of pain and the frequency with which it occurs on abdominal distension, bowel habits and Qol (33).

Nevertheless, the long-term use of this diet is still an issue (16).

3.2.1. Implementation of the Low-FODMAP diet

The introduction of a specific diet must be individualized (1). The reason for that is the existence of a great variety of IBS patients with different pathophysiology. Thus, what causes a symptom in one patient may not cause in another and therefore not all patients need to restrict all FODMAP groups. A previous anamnesis is necessary to evaluate the patients IBS symptoms (type, severity, pattern and frequency) and the habitual dietary intake (usual FODMAP intake, fibre intake, meal pattern, and suspected

trigger foods) (34). This implementation must be followed by a nutritionist because exists a high risk of diet inadequacy and developing eating disorders (1).

The LFD implementation consists of three phases: restriction phase, reintroduction phase and maintenance phase (16). In the first phase, there is a total restriction of the products that contain FODMAPs from their diets and patients are encouraged to consume foods that are low in FODMAPs (16). This phase should be applied for four to eight weeks and aims to improve symptoms (16). Then, after seeing a relief or resolution of the symptoms, patients move to the second phase, that has a duration of several weeks, approximately six to eight weeks (16). In this particular phase, patients begin the reintroduction of FODMAP sources (16). Firstly, foods that contain one type of FODMAP are gradually reintroduced over a period of two to three days (16). This phase aims to determine patients' tolerance to specific ingredients or the tolerated amount of each FODMAP and to know which symptoms are triggered by that food (16). The last phase, has as purpose to continue the intake of the fermentable carbohydrates that the patients show good tolerance (16).

3.3. Benefits of low-FODMAP diet on IBS patients

IBS is a disorder that compromises the GI function and cause several GI symptoms (1). These symptoms are associated with the decrease in Qol and with an increase in economic burden on patients, healthcare systems and the community because they tend to visit the doctor more frequently and consume more health resources (1).

Kortlever *et al.* (2019) (1), in a prospective observational study conducted among IBS patients (n=101), where it was held LFD dietary advice to evaluate the effect of the introduction of LFD at week 6 and 26 in Qol , GI and non-GI symptoms. They found that in both weeks there was an increased in IBS-related Qol (a mean 65.7 compared to a mean 72.5 in week 6 and 77.1 in week 26). Also, in this study, was seen an improvement in GI symptoms from baseline (mean 3.08) to week 6 and week 26 (mean 2.51 and 2.50, respectively), when assessed by the Gastrointestinal Symptom Rating Scale, with the exception of constipation and nausea for week 6 and for week 26, respectively, and a reduction in anxiety, depression and fatigue (1). This reduction continued until the study ended, which suggests that the implementation of the LFD on long-term has advantages on the improvement of GI symptoms (1). In another prospective study, where was studied the impact of LFD on the improvement of GI symptoms in IBS patients, who had received

dietary intervention, was observed a significant reduction of the reported symptoms such as abdominal pain, bloating, constipation, diarrhoea, nausea, compared to the baseline (2). In addition, the magnitude of this symptoms also improved (2).

In a randomized, controlled, single-blind, cross-over trial, which compared the effects of LFD and an Australian typical diet (n=38), and the only difference in both was the content in the intake of FODMAPs, being superior in LFD (35). In this study, Halmos *et al.* (2014) (35) observed a reduction in symptoms such as abdominal pain, bloating, and dissatisfaction with stool consistency, after 14 days (22.8mm) compared with baseline (36.0 mm) and the Australian diet (44.9 mm), evaluated with visual analogue scale (VAS: 0-100 mm), and this improvement was seen in 21 of 30 participants (70%), on both IBS-D and IBS-C. This affects more individuals with positive fructose malabsorption (12 of 17;70%) (35).

Staudacher *et al.* (2017) (11), evaluated the effect of LFD dietary advice compared with a sham dietary advice on symptoms on a Randomized Controlled Trial (RCT). These two diets are particularly similar but the second have a higher total FODMAP intake (17.4g/d to 9.9g/d) (11). Evaluating the total IBS symptom severity scoring system (IBS-SSS) score, was observed a lower score for the LFD (173 points) compare to the Sham Diet (224 points) and lower sub-scores for days of pain, distension severity, satisfaction with bowels and the impact of IBS symptoms on life and a higher relief in severity of all symptoms, especially abdominal pain and stool consistency (11).

Also, several studies reported the effects of the implementation of LFD vs. mNICE on IBS-D patients conducted for 4 weeks (3,36,37). Eswaran *et al.* (2016) (36) discovered that the LFD have a higher reduction on the ingestion of carbohydrates and FODMAPs comparing with mNICE. In this study, the LFD group have a higher percentage of patients that achieved the relief of IBS symptoms (52% on LFD vs. 41% on mNICE), specifically in abdominal pain, bloating, stool consistency, stool frequency and urgency (36). On a prospective, randomized, single-center, single-blind trial, where was compared the LFD and mNICE on Qol, anxiety, depression, work productivity and sleep quality in patients with IBS-D. The authors observed an improvement in bloating, stool consistency, frequency, and urgency compared to the mNICE group but these improvement was better in abdominal pain (3). Was also observed an improvement in the mean IBS-Qol score that was higher in LFD compared to the mNICE (15.9 on LFD vs 5.0 points on mNICE) (3). In the domains of anxiety, that was analysed by Hospital Anxiety and Depression

Scale, was seen a significant improvement for the subjects on LFD (9.13 to 7.73) compared to mNICE group (9.31 to 9.54) (3). Also, Staudacher *et al.* (2011) (37) discovered that the LFD group has a greater improvement for all symptoms assessed, particularly in bloating (82% on LFD vs.49% on mNICE), abdominal pain (85% on LFD vs. 61% on mNICE) and flatulence (87% on LFD vs. 50% on mNICE).

When comparing three diets (LFD, Balanced Mediterranean diet and Gluten-free diet) to evaluate the effects on GI symptoms and Qol, Paduano *et al.* (2019), in a prospective study, visualized a strong improvement in the GI symptoms. Was seen an improvement in stool solidity, evaluated with Bristol stool scale (BSC), evolving from type 6 (mild diarrhoea) to type 4 (normal stool) in all types of IBS (79%) (5). When was evaluated the abdominal bloating, abdominal pain of <24h duration and disease severity was demonstrated a decrease in all three diets (5). Regarding the Qol, it was observed an improvement for the three diets (5). The authors conclude that there are not many differences between the three diets. So, it is shown that a balanced diet that contains a proportion of FODMAPs adequately distributed during the day, that is not so restrictive and that cannot cause a nutritional inadequacy is more beneficial (5).

O`Keeffe *et al.* (2017) (32), evaluated the effects of the implementation of a long-term (6-18 months) LFD in 103 IBS patients and the patients have reported a progressive satisfactory symptom relief through the time of follow-up (61% at short-term follow-up – restriction phase vs. 57% at long-term follow-up) and 70% of these patients keep this in the long-term. Over 60% of patients reported an ameliorate of many symptoms, such as abdominal pain, bloating and flatulence and there was a reduction in patients reporting an abnormal stool frequency and consistency (32). Already in 2017, Harvie *et al.* (7), also investigated the long-term effects of the LFD in IBS patients, through a RCT (n=50). These patients were divided in two groups and the first initially had food education and the second had food education only after 3 months. Was observed, after the 3 months of intervention, a significantly reduction (272 on baseline vs 127,5 after 3 months), through IBS-SSS, on the symptoms, especially in IBS-D, and that 20 patients achieved a score <175 that is indicative of mild IBS and 3 of those reached a score <50 that is seen in healthy individuals (7). In group two, before the intervention, this was not observed, which suggests a real benefit on the implementation of LFD (7). At 6 months, in the reintroduction phase, despite the increase in the intake of FODMAPs, that improvement

was preserved (7). These participants also experienced an improvement in Qol from baseline (66 vs 81) that maintained over the 6 months (7).

Through a single-blind, randomized controlled trial (n=62), where IBS patients were split in two distinct groups: the brief advice on a commonly recommended diet group and structural individual low-FODMAP dietary advice group and followed up for 4 weeks, Patcharatrakul *et al.* (2019) (22), discovered that, after the intervention, the VAS (0-100) in the second group was significantly lower than in the first group (38,5 vs 53,5, $p<0.01$) and was seen a reduction in comparison to the baseline what did not happen in the second group.

Bohn *et al.* (2015) conducted a multi-centre single-blind randomized controlled trial in IBS patients (n=67) (38). These patients were separated in two diets, LFD and traditional IBS diet. Was found that on both diets, at the end of the intervention period, the IBS-SSS was reduced and was not seen significant differences on the efficacy between the two diets (38).

Zahedi *et al.* (2018) (39) conducted a RCT (n=101) with IBS-D comparing a LFD with a generally dietary advices followed for 6 weeks. In this trial, was observed that both diets have benefits in the improvement of the GI symptoms and Qol. However, the LFD demonstrated greater benefits on the reduction of the GI symptoms (39). In fact, the author showed that, comparing the patients after the 6 weeks, there was a decreased in IBS-SSS (LFD group: week 0=263.75/ week 6=108 vs. GDA group: week 0= 252.5/ week 6= 149.75) (39).

Moreover, on a retrospective cross-sectional study conducted with patients with IBS (n=131) and IBD (n=49), where was studied the effect of LFD on long-term adherence and on the course of the disease (40). The authors found out that 86% of the patients mentioned total or partial efficacy of dietary treatment and these percentage was higher for patients in the IBD group comparing to IBS group (42% vs. 29%) (40). Bloating (82%) and abdominal pain (71%) proved to be the more effective after LFD and besides 37% IBS patients and 24% IBD patients became asymptomatic following this diet (40). Also, has been shown that this intervention can result on the improvement in the course of the disease in patients with more severe chronic courses because was found that the number of patients with a chronic continuous disease (without periods of remission) was decreased (IBS: -25%; IBD: - 23%) at the same time that the mild indolent course (where

the disease activity disappears over time) became more prevalent (IBS: +37%; IBD: +23%) and leads to an improvement on Qol and normal stool pattern (40). In the end of the intervention, was demonstrated an improvement of stool pattern in both groups, showing an increased in the proportion of normal stools (IBS:41%; IBD: 66%) (40).

Through a controlled, single-blind parallel study (n=37), followed through 3 weeks, was observed that the patients in the LFD group reported a reduction in global symptom score of 28%, specifically abdominal pain (a reduction of 52%) and abdominal distension (41). On the contrary, in the HFD group was seen an increase of 7% on symptoms, concretely in more days of pain (41). The authors conclude that there are a correlation between the level of FODMAP consumption and the IBS symptom severity (41).

Pedersen *et al.* (2014) (42), conducted a pilot study in IBS patients (n=19), followed during 12 weeks. The authors reported that in the first 6 weeks, on the non-interventional control, compared with the baseline was seen a decreased in IBS-SSS (320 to 278) but the higher improvement was seen during the LFD period, from week 6 to week 12, (IBS-SSS: 278 to 151), improving from moderate to mild IBS severity (42). In terms of Qol, the study reported that, on the non-interventional period, was no seen any differences (baseline: 82; 6 weeks: 81) but in LFD period was seen a greater improvement (baseline:81; 6 weeks: 67) (42).

A prospective study (n=63) found out benefits on the subjective global improvement of symptoms on 80% due to implementation of LFD demonstrating a reduction in abdominal pain (85%), meteorism (73%), flatulence (69%), borborygmi (69%), fatigue (69%) and was seen an improvement in diarrhoea (11 patients) and in constipation (3 patients), measured by BSC (43). The severity of symptoms was also significantly reduced and 3 patients became symptom-free (43).

Through a randomized, cross-over trial that compare the effects of a LFD and low-lactose diet in IBS patients (n=29) and found out a significant decreased in total IBS-SSS score (-63 vs. -51 points) and showed a reduction of $\geq$ 50 points in the total IBS-SSS in 59,1% during LFD and 54,2% during LLD (23). So, these two diets proved to be efficient (23).

Cingolani *et al.* (2020) (44), investigated the effects in IBS (n=37), through the implementation of LFD, and which subtype of IBS disease could benefit more. This was an observational study and the authors observed a benefit, through the IBS-SSS and VAS

for bloating severity and pain severity. A significant reduction of severity progressing of severe intensity to mild intensity and, through the BSC, was observed a improvement but this improvement was only seen in the IBS-D group (44).

Through a randomized, double-blinded crossover study (n=20), where the participants implemented a LFD for 3 weeks, and then, after 3 weeks of washout, they were randomized to placebo group or FOS supplementation. Was observed that, after 3 weeks, an improvement in all IBS symptoms, showing a reduction in IBS-SSS, particularly for passing gas, nausea and tiredness (31). When was introduced the placebo or FOS supplementation more patients reported symptoms relief in response to placebo (80% vs 30%) (31).

All the studies mentioned above show the beneficial effect of LFD in improving symptoms associated with IBS as well as the potential positive impact on disease activity and its progression. Despite this, there are also several studies that emphasises the limitations that the LFD carries.

3.4. Limitations of low-FODMAP diet on IBS patients

Despite LFD be associated with several benefits on relieving the GI and non-GI symptoms, it is also important to consider the adverse effects of this implementation.

One problem associated with the implementation of this diet is that some patients think that following this type of diet it is too difficult (1). However, a satisfactory adherence to the diet is necessary to induce a relief on symptoms (2). So, is important to access their adherence to the diet because it is crucial to the success of the implementation. Some studies found good adherence through the implementation of LFD. In Halmos *et al.* (2014) (35), this was evaluated and was found that 80% of the IBS participants and 100% of the healthy controls was adherent to LFD, assessed by recorded food diet. In another study, was concluded that 93% followed the diet 76%-100% of the time, 7% reported that followed the diet frequently (51%-75% of the time) and no patients reported that followed the diet sometimes or never (11). This was also found in Bellini *et al.* (2017) (45) with an adherence of 98%.

Although some studies show a good adherence to this diet, others have shown otherwise. Frieling *et al.* (2019) (43), declared through a prospective study that the patients (n=63) had a low adherence because 30 patients (47%) stopped the LFD because

of ineffectiveness of diet (n=4) or nonadherence. This nonadherence was caused by the diet being too difficult and too bothersome for their normal lives (43). In other study, was seen that, at long-term follow-up, 82% of patients continued to follow the LFD. However, 86% of the patients consider that the LFD was more expensive and over 70% of patients consider that there is a great difficulty eating out at restaurants, at family and friends' house and when traveling than the habitual diet (32). Cingolani *et al.* (2020) (44), through an observational study for the implementation of LFD on 60 IBS patients, observed that 23 patients dropout. Because of that, was studied the reasons for this happen and was observed that the employment status affects the adherence to the study because the percentage of unemployment was lower in the dropouts (13%) in comparison to the treated subjects (35,2%) (44). Maagaard *et al.* (2016) (36), showed that 26% IBS patients and 20% IBD patients withdrew the LFD. The most common motives were: diet too complicated to follow (50%), too expensive (23%), bland in taste (15%) and other reasons (53%). On the other hand, a greater compliance was associated with a longer duration of dietary treatment. Furthermore, 54% followed the diet depending on the symptom severity (40). Despite that, 70% IBS patients and 55% IBD patients reported satisfaction with the dietary intervention. This satisfaction was also reported by Mclntosh *et al.* (2016) when compared to a LFD group and HFD group, showing that only those in LFD group reported a significant increased (41,45). Some authors found that the adherence on the balance diet was higher compared to the both evaluated diets (LFD and Gluten-free diet) because the LFD represents a more restrictive and expensive diet (5). Finally, Roest *et al.* (2013) (2), found that several participant did not find the diet ease to implement in their daily routine and that it is why only 12.2% of the participants reported a completed adherence to the diet. However, most participants remain adherent. Therefore, despite of the difficulties the participants consider that the improvement of the symptoms is more important (2).

The major problem is the restrictive nature of the diet (1), which promotes the low intake of a great variety of foods and nutrients. The long-term adherence may lead to nutritional deficits (29). Harvie *et al.* (2017) (7), while investigating the effects of the implementation of LFD on nutritional adequacy, observed that, in the intervention phase, was demonstrated a reduction in the energy and fibre intake, that are of high concern. However, in the reintroduction phase of FODMAPs, especially the GOS and FOS, the fibre intake increased and their amount became adequate again (7). Another study where

IBS-D patients were randomized (n=78) through two groups: mNICE and LFD group to access the effects of these diets on the mean daily nutrient content and identify nutritional inadequacy in comparison to the Dietary Reference Intakes (DRIs) (46). These diets contribute to a reduction in daily calories because they tend to have a reduction in daily meals consumed representing a fewer carbohydrate intake. In the LFD group it was possible to check a less intake of micronutrients that was only significant for the riboflavin when were adjusted for calorie intake. The authors also observed that, comparing the two diets on pre- and postintervention to the DRIs, few patients on the LFD group supplied the needs for thiamine and iron. The reason for this may be due to a reduction on the intake of fortified grains and cereals (46). Also, Staudacher *et al.* (2020) (47), in a RCT carried out in IBS-D and IBS-M (n=130) monitored for 4 weeks, comparing a LFD and a Sham Diet, the authors discovered that, in macronutrients, no difference was seen between the groups. However, in the LFD group and Sham diet was observed that a small number of patients exceed the guidelines for fat and carbohydrates. Moreover, the total starch intake was lower after the LFD intervention compared with the habitual diet (109g/day vs. 128 g/day) (47). Regarding the micronutrients, an improvement on the intake of vitamin B-12 and selenium was observed as compared to the habitual diet and sham diet, respectively, which may be due to the higher intake of fish and eggs (47). Bellini *et al*. (2017) (45), conducted a pilot study in 26 IBS patients, followed by 8 weeks, and evaluate the effect of a LFD on the nutritional status and body composition. The authors reported that the LFD caused a slightly reduction on the content of FODMAP, calories, proteins, fats, carbohydrates and fibre (45). Also, Frieling *et al.* (2019), investigate the body weigh course after the dietary intervention and found that 12 patients developed weight loss (36,7%) and 3 patients gained weight (12,2%) (43).

Other limitation on the implementation of LFD is the reduction of the gut microbiota species richness as it happens in IBD, obesity and diabetes, that are explained by the restriction of prebiotic carbohydrates. However, the effects of this reduction on clinical symptoms are unknown (11). Six studies demonstrate the effects of the implementation of LFD on the microbiota and all of them observed a reduction in Bifidobacteria. Staudacher *et al.* (2017) (11), evaluated the effect of LFD compared with the Sham Diet on faecal microbiota using quantitative PCR analysis. At follow-up, LFD reduced the absolute abundance of Bifidobacteria comparing to those patients that follow a Sham Diet (8.8 16S rRNA genes/g, SD 0.6 vs. 9.2 rRNA genes/g, SD 0.6) and that

exists a reduction in comparison with the baseline (1.70% vs 0,79% in LFD and 1.57% vs 1.93% in Sham Diet) (11). Also, Staudacher *et al.* (2020) (48), through 2×2 factorial, blinded, placebo RCT (n=95), investigate the influence of a LFD and a probiotic intervention on the microbiota (48) . These authors discovered that the LFD group had lower abundance of Bifidobacteria (0,9% vs. 2,1%), and an unclassified genus in the *Ruminococcaeceae* family (8,3% vs. 12,8%), and higher abundance of *Bacteroides* (34,1 vs. 23,3%), compared with the Sham Diet group (48). Furthermore, Bennet *et al.* (2017) (49), in a study cohort, investigate the effects of dietary intervention on gut bacteria (n=61 patients). The authors found, through the GA-map Dysbiosis Test, that the LFD was related with increased Dysbiosis scores and these scores was higher in patients that did not respond to LFD prior to the intervention and lower abundance of Bifidobacteria and Actinobacteria after the intervention (49). Also, in the study of Hustoft *et al.* (31), a reduction was observed in *Bifidobacterium*, *Clostridium*, *Faecalibacterium prausnizii*, *Megasphaera*, *Pediococcus* and Actinobacteria and an increased in *Dorea* and was also seen a decreased in n-butyric acid and SCFA and a decreased in IL-6 and IL-8. Finally, Halmos *et al.* (2015) (50), studied the effect of LFD on the reduction of the symptoms and the negative effects that the reduction of prebiotics could brought in the colonic microenvironment. This study was performed in 27 IBS patients and 6 healthy subjects through a single-blind, randomized, cross-over trial (50). These patients were randomized into the LFD or Australian diet and, after 21 days, they enter in the washout period being at their habitual diet and, after this period, they change the dietary intervention (50). During the period of follow-up, the authors observed a higher faecal pH but the concentration of SCFAs was not different between the diets (50). Was also seen that the LFD group showed a reduction in the absolute abundance of total bacteria specifically butyrate-producing bacteria, prebiotic bacteria (bifidobacteria), mucus-associated bacterium (*Akkermansia muciniphila*) and *Ruminoccocus gnavus*, and a reduction on relative abundance of A. muciniphila and *Clostridium cluster* XIVa and an increased in *Ruminococcus torques* (50). The imbalance of the gut microbiota is an adverse effect of the implementation of LFD so it can be harmful to patients.

4. Discussion

The clinical management and treatment of IBS is complex because different IBS patients can have different pathophysiology (43). So, different therapeutic strategies can be successful in one patient and in another can fail (43).

Currently, the treatment for IBS engage three common modes: dietary intervention, pharmacological and psychological therapies (51). These therapies are chosen because the purpose of the treatment is to improve the GI symptoms of IBS given that this disease is a symptom-based diagnosis (3). Notwithstanding that is an important issue, is also relevant discover the real impact in IBS-patient`s daily lives (3).

Since a large number of patients report food intake as the trigger for the worsening of symptoms, the dietary intervention has gain increasing relevance (43,52). In fact, even before the development of the FODMAPs hypothesis, restriction diets were already used (53).

The LFD was originally developed to treat patients with IBS and there is a strong body of evidence supporting the positive effects in approximately 70% of patients, much more than the results achieved with pharmacological treatment (43,53). Thus, for IBS primary care, LFD is widely recommended (43). Nonetheless, despite the benefits, this diet may cause adverse effects that need to be regarded although the clinical symptoms of these effects are not yet known (11). Furthermore, it is demonstrated by a plenty of studies that the LFD dietary advice implemented by trained nutritionists through a careful verbal and written information is crucial for the success of the relief of the IBS symptoms (38,39).

The data analysed in the present literature review demonstrate the positive effects on the overall improvement of symptoms, especially abdominal pain, bloating, flatulence and stool consistency, stool frequency and urgency (3,32,38,39). Moreover, there are a large number of studies that report that symptom relief promotes a reduction of the IBS-SSS and also the improvement in non-GI symptoms, particularly fatigue and anxiety (38–40,45). Furthermore, the use of LFD on the management of IBS can modulate the disease course and increase the remission periods (40,43). A very important discovery was that, in a randomized, double-blinded, placebo-controlled crossover study, when patients were supplemented with FOS, during LFD, the IBS symptoms got worse in comparation to a placebo supplementation which testify that FOS are a predominant factor of the onset of IBS symptoms (31). Nevertheless, this symptom level is not comparable to the symptoms observed initially. In fact, on baseline the severity of the symptoms were higher due to the fact that the intake of the other FODMAPs were kept low, which proves that the collective restriction of the FODMAPs has more benefits (31).

The adherence to the diet is an important issue for the success of the implementation and several studies reported that some patients do not continue the diet because it is not easy to implement on a daily basis, is expensive, restrictive, difficult to implement outside the home and has an unsatisfying taste and just follow depending on the severity of the symptoms (2,5,32,41,44).

Although LFD is associated with several benefits, it is important to consider that it can cause adverse effects because it is a diet in which its implementation consists of the restriction of specific foods during a defined period of time and can lead to malnutrition and weight loss (43). One of the components of food that is affected by LFD, is the fibre content. This condition can aggravate the constipation, so this diet is not very much reliable on IBS constipation predominant (IBS-C) because the decrease in fibre intake promote the reduction on the osmotic effects (1). Moreover, this decrease disturbs the fermentation of the microbiota because fibre is a prebiotic and its deprivation suppresses its growth, affect the intestinal microbiota composition and consequently the production of SCFA, that may cause an impact in the colonic mucosa and immune system (7,31).

In addition to the decrease in the fibre intake it has been reported a decrease on calorie intake, carbohydrates and fat (39,48). Therefore, during the restriction phase and in the reintroduction phase, the monitorization of the calorie and nutrient intake is of utmost importance in order to prevent malnutrition (38).

IBS patients are characterized by having a decreased intestinal microbial diversity, greater temporal instability and a relative increase of Firmicutes compared to healthy individuals (7). Thus, the implementation of a restrictive diet may aggravate changes in microbiota composition (48–50). Nevertheless, FOS supplementation has been reported to attenuate dysbiosis (60% after LFD vs 55% after FOS supplementation) (31). Some studies evaluated the implementation of FOS supplementation in IBS. However, was seen some pros and cons. The pros were that the FOS supplementation instigate the growth of Bifidobacteria and the cons were that there was no improvement on the IBS symptoms and on the contrary, an aggravation was reported (31,54).

Several studies analysed in this literature show a decrease in a specific bacteria: Bifidobacteria (11,31,41,46). This happened because this bacteria is a prebiotic bacteria and use FODMAPs as a source of energy, specially FOS and GOS (49). It is also seen a decrease in other bacteria such as: phylum Firmicutes (*Clostridium, Megasphaera, F.*

prausnitzii , *Ruminoccocus*) and *A. muciphila* (31,50). Therefore, and as expected, the supplementation with FOS cause an increase on *Bacteroides*, *Bifidobacerium*, *Actinobacteria*, *F. prausnitzii*, and *Firmicutes* (31). Furthermore, was demonstrated a decrease in the production of SCFA, metabolites like histamine and n-butyric acid and IL-6 e IL-8 (31,41). The proinflammatory cytokines and histamine are synthesized and secreted by inflammatory cells and its reduction, when the LFD is implemented, show a decreased level or activity of these cells (31), which is beneficial because it shows a reduction of the inflammatory pathways that are common in this disease The decrease of the production of n-butyric acid occur because of the reduced level or activity of butyrate-producing bacteria (31).

In conclusion, the available literature reports several benefits on the implementation of LFD in IBS patients, a positive change on disease course as well as a better Qol. Therefore, this approach is a promising strategy for clinical practice in the treatment and management of IBS. Nevertheless, possible adverse effects such as malnutrition and the impact on composition of the intestinal microbiota must be considered.

Although there is a consistent evidence regarding the LFD in IBS, the available research present limitations such as the small sample size which may impair the relevance of the results, the design of the studies, the time of diet application and several studies exclude IBS-C from the sample due to the fact that the restriction of fibre sources may exacerbate the constipation in these patients.

Further research is needed on the long-term effects of this diet especially regarding the impact on gut microbiota.

Critical Reflection

The literature described by this review withstand the positive effects associated with implementation of LFD in IBS patients. This diet has a strong potential to the management of IBS in clinical practice especially through the relief of GI and non-GI symptoms, such as fatigue and anxiety, and improved Qol. However, individualization and constant monitorization is of utmost importance in order to avoid negative consequences. It is also important that professionals explain to patients all the steps of the diet implementation since the better patients understand the diet, more effective this approach will be.

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6. Figures/ Tables

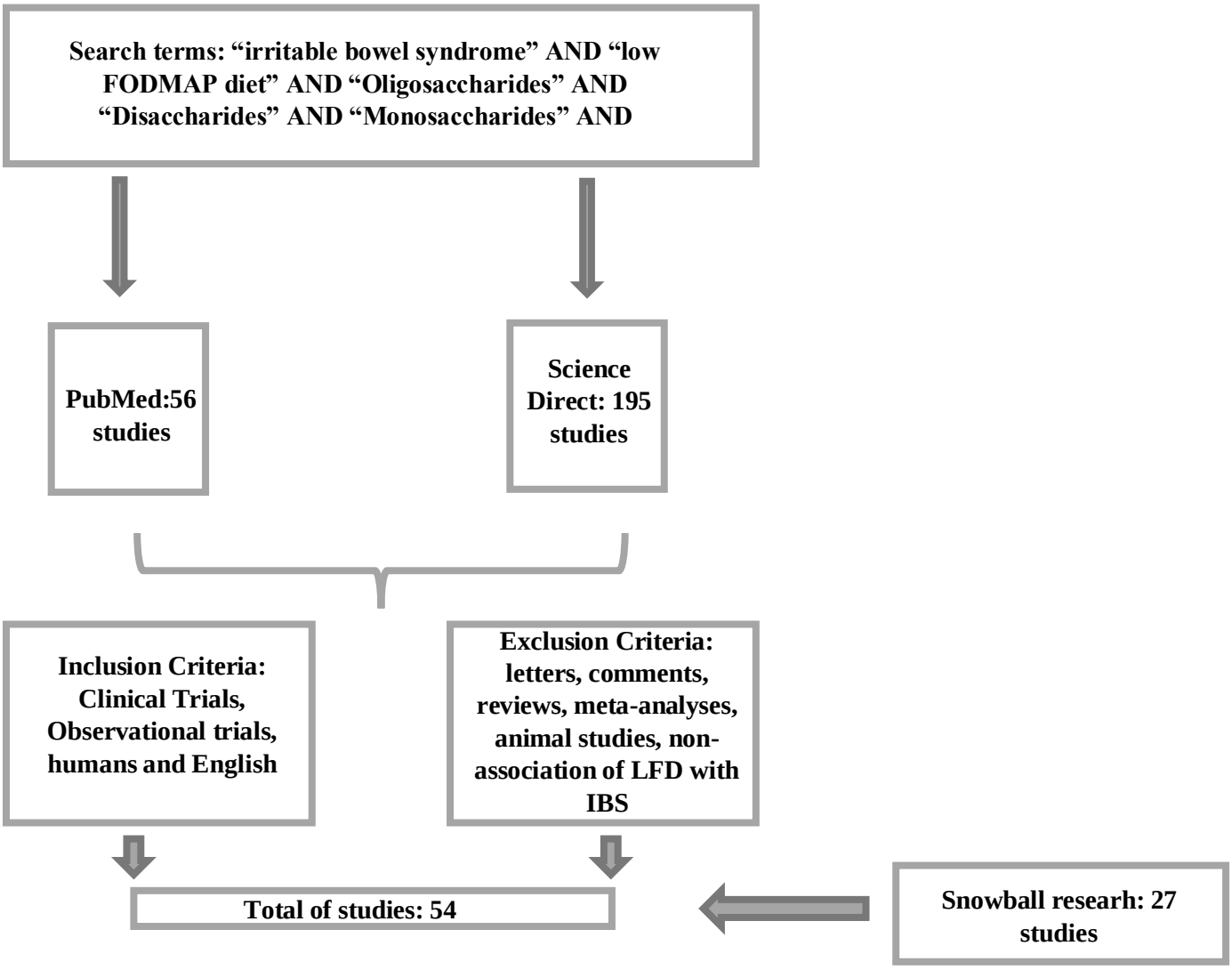

Figure 1. Fluxogram where are described the search terms used and the final studies used for this review.

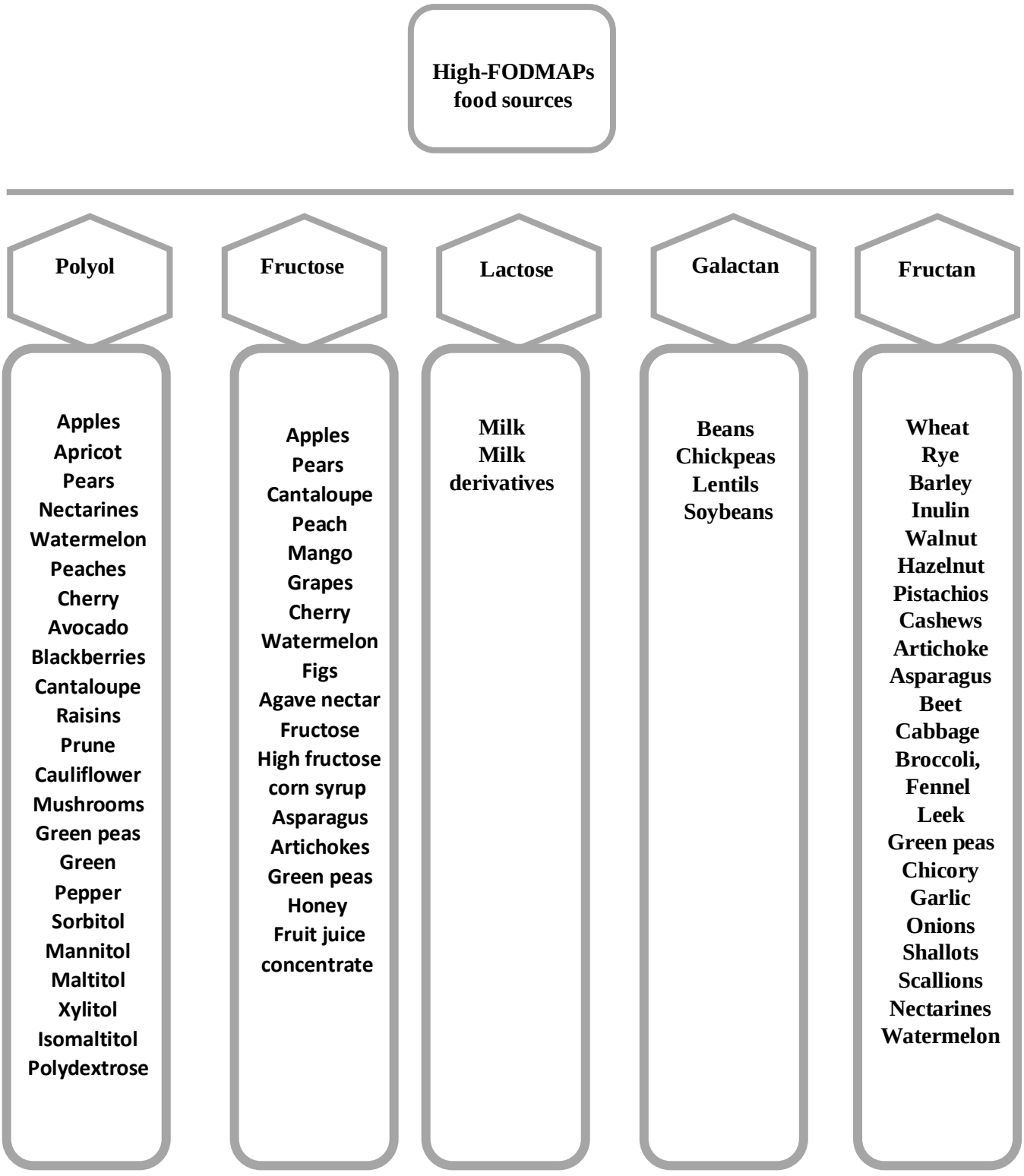

Figure 2. High Fermentable Oligosaccharides, Disaccharides, Monosaccharides, and Polyols (FODMAP) sources. Adapted from Cingolani, A. et al (2020). Feasibility of Low Fermentable Oligosaccharide, Disaccharide, Monosaccharide, and Polyol Diet and Its Effects on Quality of Life in an Italian Cohort. Nutrients (32).

Table 1. Summary of the reported results regarding LFD as an intervention on IBS

Author (Year)	Country	Sample	Intervention	Study Design	Findings
Kortlever *et al.* (2019)	New Zealand	101 IBS patients	LFD	Prospective Observational study	LFD cause an improvement on GI symptoms from baseline (mean 3.08) to week 6 (mean 2.51) and week 26 (mean 2.50), except constipation and nausea. This reduction continued until week 26.
Halmos *et al.* (2014)	New Zealand	38 (30 with IBS; 8 healthy controls)	LFD vs. Australian Diet	RCT, single-blind, cross-over	Lower overall GI symptoms (abdominal pain, bloating, passage of wind, dissatisfaction with stool consistency) on LFD (22.8mm) vs a Australian Diet (44.9mm). This improvement was seen in 70% of participants.
Staudacher *et al.* (2017)	United Kingdom	104 IBS patients	LFD vs. Sham Diet	RCT	LFD induced a higher reduction in mean IBS-SSS score than Sham Diet (173 vs. 224, respectively) LFD has a trend toward adequate relief (57%) vs. Sham Diet group (38%). A higher relief in severity of all symptoms, especially abdominal pain and stool consistency)
Roest *et al.* (2013)	New Zealand	90 IBS patients	LFD	Prospective Observational study	LFD resulted in a reduction of the reported symptoms (abdominal pain, bloating, constipation, diarrhoea, nausea, passing gas, loose bowel movements, hard stools, urgent need for bowel movement, feeling not completely emptied after bowel movement)
Eswaran *et al.* (2017)	United States of America	84 IBS-D patients	LFD vs traditional dietary recommendations	Prospective, randomized, single-centre, single-blinded trial	LFD show adequate relief of symptoms (52%) compared to mNICE (41%), especially abdominal

					pain, bloating, stool consistency, stool frequency and urgency
Paduano *et al.* (2019)	Italy	28 IBS patients	LFD vs. Gluten-free diet vs. Mediterranean diet	Prospective study	The authors visualized a strong improvement on GI symptoms and on the severity of the disease in the three diets
O`Keefe *et al.* (2017)	United Kingdom	103 IBS patients	LFD	Prospective study	LFD show adequate relief of symptoms (abdominal pain, bloating and flatulence), both short- term (61%) and long-term (57) and 70% of these participants keep this improvement in long-term.
Harvie *et al.* (2017)	New Zealand	50 IBS patients	LFD	RCT	After 3 months of follow-up was observed a decreased in IBS-SSS comparing LFD vs baseline (127,5 vs 272), especially IBS-D.
Hustoff *et al.* (2016)	Norway	37 IBS patients	LFD vs HFD	Randomized, double-blind, placebo-controlled crossover study	Three weeks of LFD resulted in a significantly decreased in IBS-SSS and overall symptoms, especially abdominal passing gas, nausea and tiredness
Bohn *et al.* (2015)	Sweden	67 IBS patients	LFD vs traditional dietary recommendations	Multi-centre, parallel, single-blind study	Was seen a decreased in the severity of symptoms. However, was not seen significant differences on the efficacy between the two diets.

IBS: Irritable Bowel Syndrome; IBS-D: IBS Diarrhoea predominant; LFD: Low-FODMAP (Fermentable Oligo-, Di-, and Monosaccharides and Polyols) Diet; HFD: High-FODMAP Diet; RCT: Randomized controlled trial; GI: Gastrointestinal; IBS-SSS: instrument scores symptom severity on visual analogue scale items and where the scale is between 0 and 500 points, which means the worst severity