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Lactose Intolerance and Osteoporosis Development in Irritable Bowel Syndrome Patients

İrritabl Bağırsak Sendromlu Hastalarda Laktoz İntoleransı ve Osteoporoz Gelişimi

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ABSTRACT

Irritable bowel syndrome (IBS) is one of the most common chronic functional disorders among gastrointestinal system diseases. IBS, which has a high prevalence worldwide, negatively affects the quality of life of patients. The mechanisms that are effective in the development of IBS has not clearly been defined. However, its mechanism is thought to be multifactorial. IBS is characterized by certain symptoms, such as abdominal pain, diarrhea, constipation, flatulence, and indigestion. Nevertheless, these symptoms aren't specific to IBS and can often be confused with lactose intolerance (LI) symptoms. On the other hand, the probability of having LI at the same time is quite high in IBS patients. IBS patients restrict lactose-containing foods, especially milk and dairy products, due to the thought that they trigger their symptoms, and thus calcium deficiency may occur as a result. Due to insufficient calcium intake for a long time, the risk of osteoporosis and osteoporotic fractures becomes an important problem. In line with all these factors, this review aims to examine osteoporosis that may develop due to the presence of LI in IBS patients and to make nutritional recommendations.

Keywords*: Nutritional treatment, Irritable bowel syndrome, Lactose intolerance, Osteoporosis*

ÖZET

İrritabl bağırsak sendromu (IBS), gastrointestinal sistem hastalıkları arasında en sık görülen kronik fonksiyonel bozukluklardan biridir. Dünya genelinde prevalansı yüksek olan IBS, hastaların yaşam kalitesini olumsuz yönde etkilemektedir. IBS'nin gelişiminde etkili olan mekanizmalar tam olarak anlaşılamamıştır. Ancak mekanizmasının multifaktöriyel olduğu düşünülmektedir. IBS, karın ağrısı, ishal, kabızlık, gaz ve hazımsızlık gibi belirli semptomlarla karakterizedir. Bununla birlikte, bu semptomlar IBS'ye özgü değildir ve sıklıkla laktoz intoleransı (LI) semptomları ile karşılaşılabilmektedir. Öte yandan İBS hastalarında aynı anda LI görülme olasılığı oldukça yüksektir. IBS hastaları, semptomlarını tetikledikleri düşüncesiyle laktoz içeren gıdaları özellikle süt ve süt ürünlerini kısıtlamakta ve bunun sonucunda kalsiyum eksikliği oluşabilmektedir. Bu hastaların uzun süre yetersiz kalsiyum alması sonucunda osteoporoz ve osteoporotik kırık riski önemli bir sorun haline gelmektedir. Tüm bu faktörler doğrultusunda bu derleme, İBS hastalarında LI varlığına bağlı olarak gelişebilecek osteoporozu incelemeyi ve beslenme önerilerinde bulunmayı amaçlamaktadır.

Anahtar Kelimeler*: Beslenme tedavisi, İrritabl barsak sendromu, Laktoz intoleransı, Osteoporoz*

INTRODUCTION

Irritable bowel syndrome (IBS) is a functional gastrointestinal (GI) health problem that is clinically characterized by some symptoms without an underlying disease (Torres et al., 2018). The pathophysiology of IBS has not clearly been defined, but a multifactorial mechanism is thought to be involved, including intestinal barrier disruption, intestinal motility alteration, microbiota disorder, immune system, visceral hypersensitivity, and changes in enteric nervous system/central nervous system interactions (McKenzie et al., 2012; Algera, Colomier, & Simrén, 2019; Silva et al., 2019; Wongtrakul, Charoenngam, & Ungprasert, 2020). In addition to these, it's thought that genetic factors, age, gender, diet, stress, some infections, and some drugs may be effective in the development of IBS (Chey, Kurlander, & Eswaran, 2015).

IBS is quite common all over the world and its prevalence has been reported to be 11.2%. Additionally, it's thought to vary between 1.1-45% according to countries and regions, depending on the diagnostic method used (Lovell & Ford, 2012). The prevalence of IBS was found to be 10-15% in Europe and North America, 13.5% in Sweden, 5.7% in China, 14% in Pakistan, and 22.1% in Taiwan (Quigley et al., 2016). The number of studies examining the prevalence of IBS in Türkiye is quite limited. However, it was found to be 6.3% in one of the previous studies using the Rome II criteria (Celebi et al., 2004) and 19% in the other (Özden et al., 2006).

Diagnosis of IBS primarily requires the exclusion of some diseases such as colon cancer, celiac disease, inflammatory bowel disease, rectal bleeding/melena, and unexplained anemia (Chey et al., 2015). It's diagnosed using various diagnostic criteria developed specifically for IBS (Silva et al., 2019). Rome IV criteria are generally used as the current diagnostic standard. According to the Rome IV criteria, the diagnosis of IBS is clarified if two of the following criteria are present with abdominal pain recurring at least one day a week in the last three months, in addition to the fact that it started at least six months before the diagnosis (Black & Ford, 2020);

•Decrease with defecation

•Accompanied by changes in the frequency of defecation

•Accompanied by a change in stool consistency

IBS reduces the quality of life of patients by causing GI symptoms such as abdominal pain and discomfort, constipation or diarrhea, indigestion, flatulence and bloating, as well as fatigue, insomnia, and anxiety (Casellas et al., 2018; Silva et al., 2019; Chey, Keefer, Whelan, & Gibson, 2021). However, these symptoms aren't specific to IBS patients. Food intolerances, particularly lactose intolerance (LI), have symptoms like IBS, and these two conditions can be confused or co-occurring (Silva et al., 2019; Cancarevic, Rehman, Iskander, Lalani, & Malik, 2020). Accordingly, patients try to prevent their symptoms by avoiding the consumption of milk and dairy products (Xiong, Wang, Gong, & Chen, 2017). Some nutrient deficiencies may occur due to the excessively restrictive diet of IBS patients for a long time, and this may result with health problems such as osteoporosis (Cozma-Petruț, Loghin, Miere, & Dumitrașcu, 2017).

In this review, it is aimed to examine the osteoporosis that may occur as a result of restriction of the intake of certain foods in IBS patients with LI and to give nutritional recommendations.

Lactose Intolerance

Lactose intolerance (LI) is a clinical condition that develops as a result of an insufficient breakdown of lactose into monosaccharides due to lactase enzyme deficiency in the small intestine (Malik & Panuganti, 2021). Unmetabolized lactose passes into the colon and is fermented by bacteria to products such as short-chain fatty acids, hydrogen (H_2), methane (CH_4), and carbon dioxide (CO_2) gases (Yang et al., 2015). These products cause symptoms such as abdominal pain, flatulence, cramps, bloating, diarrhea, and fatigue that occur within 30 minutes or a few hours after consumption of lactose-containing foods in individuals with LI (Campbell et al., 2010; Kumar, Ranjan, Mittal, Singh, & Ghoshal, 2012; Jansson-Knodell, Krajicek, Savaiano, & Shin, 2020). The main method used in the diagnosis of LI is the hydrogen breath test, which is a non-invasive method that provides objective information about the digestion and absorption of lactose (Yang et al., 2015).

LI is a very common food intolerance worldwide and affects approximately 70% of the world's population (Cancarevic et al., 2020). The prevalence of LI varies widely between countries

and regions. While it's seen at a rate of 5-17% in Northern European and American countries, this rate can reach over 50% in South American, African, and Asian countries and 100% in some Asian countries (Lomer, Parkes, & Sanderson, 2008). Although there is not enough study to determine the prevalence of LI in Turkiye, it's thought that the prevalence of lactase deficiency in adults is approximately 70% (Mądry & Fidler, 2010).

LI is classified into three subtypes: Congenital LI, which is rarely seen and congenital, Primary LI which occurs with the decrease in lactase enzyme secretion in adults with aging, and Secondary LI which develops due to various diseases especially affecting the intestines (Casellas et al., 2018).

Lactose Intolerance in Irritable Bowel Syndrome

IBS patients associate the appearance or increase of symptoms with the consumption of various foods (Monsbakken, Vandvik, & Farup, 2006; Xiong et al., 2017). It has been reported that the symptoms seen in IBS patients are triggered by the consumption of foods rich in oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs), which can be fermented by colon bacteria (Solar et al., 2019). Lactose is defined as one of the FODMAPs nutrients in individuals with LI (Zhu et al., 2013; Deng, Misselwitz, Dai, & Fox, 2015). In a study by Lee et al (2019), it was reported that the presence of food intolerance in IBS patients has a very high rate of 79.2%. In addition, it was determined that 63.4% of IBS patients developed an intolerance to FODMAPs, and 15% to milk and dairy products.

Because the symptoms of IBS and LI are quite similar, they are often confused with each other, and this can make diagnosis difficult (Dabak et al., 2019; Silva et al., 2019). However, according to the results of a meta-analysis, it was determined that the frequency of co-existing LI in IBS patients is quite high (Varjú et al., 2019). The prevalence of LI in IBS patients is thought to vary between 17-86% (Almazar et al., 2019). In the study conducted by Zhu et al. (2013) LI was found to be 53.8% in IBS patients, while this rate was 28.1% in individuals in the control group. In the study of Xiong et al. (2017) with IBS-D patients, self-reported intolerance to milk and products was determined as 53% in IBS patients with LI and 37% in IBS patients without LI. In a study conducted by Dabak et al. (2019) in Turkiye, the prevalence of LI was found to be 47% in IBS patients, while it was found to be 23% in the control group.

Although IBS patients often report experiencing symptoms of LI, patient-reported intolerance status doesn't always correlate with the results of objective tests, such as the hydrogen breath test (Zhu et al., 2013; Cozma-Petruţ et al., 2017).

Osteoporosis

Osteoporosis is a metabolic bone abnormality characterized by decreased bone mass, disruptions in bone microstructure, and increased bone fragility (Yen et al., 2014). The main risk factors for the development of osteoporosis are age, gender, menopause, family history, insufficient calcium consumption/absorption, vitamin D deficiency, sedentary life, weight loss, smoking, alcohol, malnutrition, some drugs, and some diseases (Yen et al., 2014; H. S. Lee et al., 2018; Wongtrakul et al., 2020). In addition, lower intake of nutrients such as protein, potassium phosphorus, and magnesium can lead to bone metabolism abnormalities (Hodges, Cao, Cladis, & Weaver, 2019).

Osteoporosis is quite common in the general population and is mostly seen in 10% of individuals over 50 years of age and 25% of individuals over 80 years of age (Wongtrakul et al., 2020). According to the results of a meta-analysis conducted in the Eastern Mediterranean Region, it was reported that the incidence of osteoporosis in this region is 24.4% and it's increasing every year (Zamani, Zamani, Heidari, Parsian, & Esmaeilnejad-Ganji, 2018). In a study conducted in Turkiye (Alkan, Fidan, Tosun, & Ardıçoğlu, 2011), the prevalence of osteoporosis in women was reported as 7.61% and the rate of development of osteoporosis in women was found to be 5 times higher than in men.

Osteoporosis in Irritable Bowel Syndrome

In particular, individuals with inflammatory bowel disease have a 40% higher risk of osteoporosis and osteoporotic fractures compared to the general population (Ali, Lam, Bronze, & Humphrey, 2009). In the development of osteoporosis in IBS patients, bone destruction caused by inflammatory cytokines such as IL-1, IL-17, TNF-alpha, and nutrient absorption disorders are thought to be effective (Bianchi, 2010; Stobaugh, Deepak, & Ehrenpreis, 2013). The fact that most IBS patients avoid the consumption of milk and dairy products, not only during the presence of symptoms but also when there are no symptoms, is an important problem that causes chronic calcium deficiency

(Jackson & Savaiano, 2001; Bianchi, 2010; McKenzie et al., 2012; H. S. Lee et al., 2018).

The study by Torres et al. (2018) showed that IBS patients consume less milk and dairy products and have significantly lower calcium intakes compared to a healthy control group. In a meta-analysis study by Wongtrakul et al. (2020), it was reported that IBS patients had a 1.95 times higher risk of developing osteoporosis and 1.58 times more risk of osteoporotic fractures than individuals without IBS. Similarly, Yen et al. (2014) reported that there is a higher incidence of osteoporosis in IBS patients than in those without IBS and that the risk of developing osteoporosis is higher in female patients aged 40-59 years. In addition, it has been determined that the risk of developing osteoporosis is 2.18 times higher in female patients under the age of 40 compared to men. The study of Lee et al. (2018) reported that the risk of osteoporotic fractures is 1.27 times higher in IBS patients than in the control group.

In line with the studies conducted, it has been shown that there is a significant increase in the risk of osteoporosis in IBS patients. Despite this, it has been reported that these patients are not adequately screened for osteoporosis (Shah-Khan, Cumberledge, Shah-Khan, Gannon, & Kupec, 2019).

Nutritional Recommendations

Treatment of IBS is primarily aimed at improving or reducing symptoms due to the incomplete understanding of the underlying pathophysiological conditions, and the role of medical nutrition therapy has gained great importance in recent years (Cozma-Petruţ et al., 2017; Le Morvan de Sequeira, Kaeber, Cekin, Enck, & Mack, 2021).

Medical nutrition therapy for IBS patients is directed in two stages. In the first stage, it's aimed to provide individuals with healthy eating and lifestyle habits along with recommendations to limit the consumption of alcohol, cigarettes, caffeine, spicy, fatty, and gas-causing foods, and to increase fluid consumption and physical activity (Compston, 2013; Casellas et al., 2018; Lopes, Miszputen, Sachs, Lima, & Ambrogini, 2019). In the second stage of medical nutrition therapy, the low-FODMAP diet, which has come to the fore in recent years, can be applied. According to the low-FODMAP diet, consumption of oligosaccharides, disaccharides, monosaccharides, and polyols are restricted for 4-8 weeks and then gradually added back to the diet according to the tolerance status of the patients and the severity of the symptoms (Casellas et al., 2018; Bellini et al., 2020). Thus, 50-80% of symptoms are reduced in IBS patients (Misselwitz, Butter, Verbeke, & Fox, 2019). However, it's very important not to apply low FODMAP nutrition for longer than recommended and to maintain it under the control of a dietitian (Cozma-Petruţ et al., 2017).

As mentioned in the previous sections, LI is a very common condition in IBS patients (Casellas et al., 2018). However, if IBS patients are only diagnosed with LI, low lactose medical nutrition therapy is recommended. On the other hand, sometimes an objective diagnosis of LI cannot be made due to the negative results of diagnostic tests. In such a situation, if there is still a suspicion of intolerance to milk and dairy products, low lactose medical nutrition therapy may be recommended (McKenzie et al., 2012). In a low-lactose diet, patients should avoid the consumption of certain foods such as milk, yogurt, butter, cheese, cream, ice cream, and packaged foods (Facioni, Raspini, Pivari, Dogliotti, & Cena, 2020). It should be noted that restricting especially milk and dairy products will cause a decrease in the intake of some nutrients such as calcium, potassium, B vitamins, and protein (Savaiano, 2011). This is a significant risk for the development of osteoporosis in IBS patients (Vernia et al., 2014; Casellas et al., 2018).

It's recommended to use lactose-free milk and dairy products or to consume beverages such as rice milk, almond milk, oat milk and coconut milk fortified with calcium and vitamin D to prevent nutritional deficiencies and the development of osteoporosis in IBS patients with LI (Ratajczak, Rychter, Zawada, Dobrowolska, & Krela-Kaźmierczak, 2021). On the other hand, these drinks also contain components that prevent calcium absorption such as phytate and oxalate, and there is no clear data on bioavailability levels (Hodges et al., 2019). In addition, it may be recommended to increase the consumption of green leafy vegetables, which are a source of calcium, but they should be consumed with caution in IBS patients as these products can be difficult to digest (Ratajczak et al., 2021).

Symptoms of LI usually depend on the amount of lactose intake, and consuming about 12 grams of lactose per day (1 serving = 200-250 ml milk/yogurt or 30-50 g hard cheese) in patients

triggers symptoms less (Cozma-Petruţ et al., 2017; Misselwitz et al., 2019). Further, it's thought that the probiotic bacteria in yogurt may have a beneficial effect by providing the passage of lactase enzyme to the small intestines (Staudacher, 2015). Since the amount of lactose decreases in fermented cheeses, the consumption of traditionally prepared hard cheeses is also recommended (Casellas et al., 2018). For all that, it's thought that probiotic supplements will also have a beneficial effect and reduce symptoms (Ratajczak et al., 2021). As a result, in IBS patients with LI, possible nutrient deficiencies can be prevented by consuming dairy products such as milk-yogurt or fermented cheese in small amounts and spreading them throughout the day along with other nutrients (Hodges et al., 2019). If necessary, it's very important to provide calcium and vitamin D supplements to patients with calcium deficiency and who are at risk for the development of osteoporosis and to screen these individuals regularly (Bianchi, 2010).

CONCLUSION and RECOMMENDATIONS

The prevalence of LI in IBS patients is quite high, and it's worrisome that patients restrict lactose-containing foods to prevent symptoms that may cause deficiencies of nutrients that are essential for bone health. It's reported that the risk of osteoporosis is generally quite high in IBS patients. However, the pathophysiology of LI and osteoporosis in IBS patients aren't clearly defined, and there is a lack of studies examining these factors together. In addition, despite the increasing importance of nutritional therapy in the management of IBS symptoms in recent years, there isn't enough evidence about the long-term effects of nutritional therapy. Therefore, to prevent health problems such as osteoporosis that may develop due to unconscious restriction of food intake in IBS patients, medical nutrition therapy should be provided under the control of a dietitian. In addition, it's very important to regularly screen for possible risk factors in a multidisciplinary team. In conclusion, there is a need for more comprehensive studies examining the development of LI and osteoporosis together in IBS patients.

Author Contributions

Idea/Concept: M.A., A.A.P.; Design: M.A., A.A.P.; Supervision/Consulting: A.A.P.; Analysis and/or Interpretation: M.A., A.A.P.; Literature Search: A.A.P.; Writing the Article: M.A., A.A.P.; Critical Review: A.A.P.

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Conflict of Interest

The author declared that there was no conflict of interest in the conduct of the research.

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