



Comparative Evaluation of Lactulose and Bisacodyl in the Management of Chronic Constipation: Efficacy, Safety, and Patient Preferences

Kronik Kabızlık Yönetiminde Laktüloz ve Bisakodilin Karşılaştırmalı Değerlendirmesi: Etkinlik, Güvenlik ve Hasta Tercihleri

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Abstract

Chronic constipation is a common gastrointestinal disorder, and its management often requires long-term use of laxatives. This review addresses the differences between two commonly used laxatives, lactulose and bisacodyl. The efficacy, side effect profiles, tolerance development, use in special populations, drug interactions, contraindications, and impacts on patient compliance and quality of life of these two laxatives are compared. Both lactulose and bisacodyl are effective in improving bowel movements and are widely used in clinical practice. However, lactulose might present a more favorable profile for certain patient populations when considering factors such as side effect profile, patient compliance, quality of life, and cost-effectiveness. Primary care physicians should consider these aspects when choosing the most appropriate treatment option for their patients, always considering individual patient characteristics and preferences.

Keywords: Bisacodyl, constipation, lactulose, laxative, osmotic, purgative, stimulant

Öz

Kronik kabızlık, yaygın bir gastrointestinal bozukluktur ve yönetimi genellikle laksatiflerin uzun süreli kullanımını gerektirir. Bu derlemede, yaygın olarak kullanılan iki laksatif olan laktüloz ve bisakodil arasındaki farklılıklar ele alınmıştır. Her iki laksatif etkinlik, yan etki profili, tolerans gelişimi, özel popülasyonlarda kullanım, ilaç etkileşimleri ve kontrendikasyonları, hasta uyumu ve yaşam kalitesi üzerindeki etkileri yönünden var olan kanıtlar ışığında karşılaştırılmıştır. Hem laktüloz hem de bisakodil, bağırsak hareketlerini iyileştirmede etkili olup klinik uygulamada yaygın olarak kullanılırlar. Ancak, yan etki profili, hasta uyumu, yaşam kalitesi ve maliyet-etkinlik gibi faktörler göz önüne alındığında, laktüloz belirli hasta popülasyonları için daha olumlu bir profil sunabilir. Aile hekimleri, hastaları için en uygun tedavi seçeneğini seçerken bu yönleri göz önünde bulundurmalı ve her zaman bireysel hasta özelliklerini ve tercihlerini dikkate almalıdırlar.

Anahtar kelimeler: Bisakodil, kabızlık, laksatif, laktüloz, müshil, osmotik, uyarıcı

Introduction

Constipation is a common condition encountered in primary care, with a reported prevalence of up to 27% in North America and Europe (1). It is characterized by

infrequent bowel movements, hard stool consistency, and difficulty or straining during defecation. Chronic constipation can significantly impair the quality of life, posing both a physical and psychological burden on patients (2).



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The management of constipation often includes lifestyle modifications such as increased dietary fiber and fluid intake, regular exercise, and over-the-counter laxatives. Among these, lactulose and bisacodyl are two widely prescribed laxatives. Lactulose is an osmotic laxative that draws water into the colon to soften stools and stimulate bowel movements (3). Bisacodyl, on the other hand, is a stimulant laxative that promotes intestinal motility by directly stimulating the enteric nerves of the colon (4).

Despite their everyday use, there remains a need for more consensus in primary care regarding the optimal laxative for treating constipation. This narrative review aims to compare lactulose and bisacodyl regarding efficacy, safety, patient preference, and cost-effectiveness, focusing on evidence from clinical studies published in medical journals.

Pharmacological Overview

Lactulose and bisacodyl represent two distinct classes of laxatives: osmotic and stimulant laxatives. These two types of laxatives operate through different mechanisms within the gastrointestinal tract.

Lactulose is a synthetic disaccharide not absorbed in the small intestine due to the lack of appropriate enzymes. Upon reaching the colon, it is metabolized by bacterial flora into low molecular weight organic acids, primarily lactic acid and small amounts of formic and acetic acids (5). This metabolic process increases the osmotic pressure within the bowel, leading to an influx of water that softens the stool and promotes peristalsis (6). The acidification of the colonic contents also stimulates the growth of beneficial, acid-loving bacteria while inhibiting the growth of potentially pathogenic, ammonia-producing bacteria. This makes lactulose particularly beneficial for patients with hepatic encephalopathy, where it is used to reduce blood ammonia levels (7).

Bisacodyl is a diphenylmethane derivative and functions as a stimulant laxative. It works locally on the colon to stimulate peristalsis and the accumulation of water and electrolytes within the intestinal lumen (8). After oral administration, bisacodyl is metabolized in the small intestine and colon to form the active compound bis-(p-hydroxyphenyl)-pyridyl-2 methane, which stimulates the nerves of the colonic wall, increasing the movement of the intestines (4). Bisacodyl is known for its rapid onset of action, often producing a bowel movement within 6 to 12 hours of administration (9).

While bisacodyl is effective in stimulating bowel movements, its mechanism of action can cause cramping and discomfort due to increased peristalsis. Additionally, it can affect electrolyte balance within the colon, leading to potential electrolyte imbalances if used excessively (9). In contrast, lactulose's osmotic action offers a gentler, more physiologic method for promoting bowel movements. While it may take longer to produce a bowel movement than bisacodyl, its side effect profile is generally milder and includes less risk of causing electrolyte imbalances (10).

It's crucial to note that while lactulose and bisacodyl are effective for relieving constipation, their different mechanisms of action may be more suitable for different types of patients or specific clinical scenarios. The choice between lactulose and bisacodyl will ultimately depend on individual patient factors, the specific clinical scenario, and the overall treatment goals. The following sections will provide a more in-depth look at their comparative efficacy, safety, and patient preferences.

Clinical Efficacy and Side Effect Profile

The clinical efficacy of a laxative is generally assessed based on its ability to improve bowel movement frequency, ease of defecation, and stool consistency. Both lactulose and bisacodyl have demonstrated efficacy, but several studies suggest differences in their performance and applicability to specific patient groups. Side effects play a substantial role in patient adherence to treatment, especially when dealing with chronic conditions like constipation. Both lactulose and bisacodyl have distinct side effect profiles that should be considered.

Lactulose, as an osmotic laxative, has long been studied in extensive trials in adults and children and has consistently been shown to alleviate constipation symptoms (3). Lactulose is exceptionally well tolerated. Nearly no absorption from the intestines and the rapid excretion of the absorbed portion from the kidneys results in almost all reported side effects being mild and limited to the gastrointestinal system (11). These effects include bloating, gas, and, less frequently, nausea and diarrhea (3). It has been shown that these effects decrease as the body adapts to the medication with continued use (5). No clinically significant lactulose toxicity has been reported, and no evidence of toxicity has been found in animal studies. Warnings exist about rare allergic reactions in those with milk allergy and the potential triggering of lithium toxicity through dehydration in psychiatric patients taking lithium (11). A randomized controlled trial comparing lactulose

with a senna-fiber combination in elderly patients with long-standing chronic constipation demonstrated that lactulose was as effective as the senna-fiber combination in increasing bowel movement frequency and improving stool consistency but with fewer side effects (10). Due to this efficacy, it should be considered in the third-line treatment after lifestyle changes and increased fiber intake, especially in patients with chronic constipation (12). One of its most important effects is its use as a cornerstone in treating nearly hepatic encephalopathy due to reducing ammonia absorption via several different mechanisms (11). It decreases the formation of cholesterol stones by speeding up transit time. Recent studies have reported that lactulose exhibits anti-cancer effects by binding to galectins, carbohydrate-binding proteins known to play a role in tumor progression (13).

Bisacodyl, as a stimulant laxative, typically acts faster than lactulose, but on the other hand, has a different set of potential side effects due to its stimulant nature. A study by Kienzle-Horn et al. (4) demonstrated that bisacodyl produced a bowel movement within 6 to 12 hours of administration, indicating its particular utility for patients requiring quick relief. However, the same study also showed that bisacodyl was associated with severe abdominal cramps in some patients, which limits its acceptability and long-term use. Other side effects include diarrhea and electrolyte imbalance, which is mainly a problem in the elderly with excessive use (8). Kamm et al. (14) conducted a randomized, double-blind, parallel-group study at 27 centers in the US to compare bisacodyl with placebo. They thoroughly examined its efficacy as well as its side effect profile (14). Of the patients in the bisacodyl group, 17.8% (n=44/247) could not continue the study due to various side effects, primarily diarrhea, upper abdominal pain, and headache. Half of the patients reported good tolerance of bisacodyl (14). According to a report prepared in 2005 by the American College of Gastroenterology Association Chronic Constipation Task Force, which has not yet been updated, there is not enough evidence of sufficient strength to support the use of stimulant laxatives like bisacodyl, stool softeners, herbal supports, and lubricants, while there is A-level evidence for the efficacy of osmotic laxatives like lactulose, polyethylene glycol, and tegaserod (15). Effects shown in animal studies, such as the damage to the myenteric plexus and smooth muscle, and colon dilation caused by the chronic use of stimulant laxatives, and triggering transitional cell carcinoma in the bladder epithelium of mice have not been demonstrated in humans (16). A limited number of publications related

to its association with complications such as salt loading, hypokalemia, and protein-losing enteropathy (17). In chronic use, high dosage results in severe diarrhea and toxicity due to electrolyte disorders, including hypokalemia, hypocalcemia, metabolic acidosis, or alkalosis. It has also been reported to cause renal calculus formation at levels that block double-J stents in overdose (16). Due to the unclear long-term effects of bisacodyl and the potential carcinogenic risks of stimulant laxatives, avoiding use for more than four weeks is recommended until these points are clarified with epidemiological studies (18).

Both lactulose and bisacodyl have minimal drug interactions. However, lactulose may reduce the absorption of other oral drugs when taken concurrently due to its effect on bowel motility (19). Lactulose is contraindicated in patients with galactosemia. On the other hand, bisacodyl may enhance the effects of diuretics and corticosteroids, leading to an increased risk of electrolyte imbalance (20). Both drugs should not be used in patients with ileus, acute surgical abdomen, or severe dehydration (20).

In summary, while both lactulose and bisacodyl generally have well-tolerated side effect profiles, the milder side effect profile of lactulose, lower risk of diarrhea, lower risk of electrolyte imbalance, proven efficacy and safety in long-term treatment mainly make lactulose a more appropriate choice in patients with chronic constipation, candidates for long-term use, elderly, and those with comorbidities.

Tolerance Development

Tolerance development to medications is a crucial factor, especially for conditions requiring long-term management, such as chronic constipation.

Lactulose is a non-stimulant laxative, and it has been demonstrated in multiple studies that patients do not develop tolerance to lactulose with long-term use. Its effectiveness remains consistent over time, even with continuous use (21).

In contrast, the available literature suggests that with long-term use, some patients may develop a tolerance to bisacodyl and other stimulant laxatives. This tolerance could necessitate higher doses to achieve the same effect, potentially increasing the risk of side effects such as abdominal discomfort and electrolyte imbalances (8). However, it's worth noting that this effect is not seen in all patients and can vary significantly.

Therefore, when considering treatment for long-term use in managing chronic constipation, lactulose may

offer advantages in terms of consistent efficacy without developing tolerance.

Use in Special Populations

Special populations such as the elderly, children, and pregnant women often require careful consideration when prescribing medication.

Lactulose has been widely used across all age groups, including children and the elderly, and is generally considered safe during pregnancy (22). Its sweet taste and the availability of a liquid formulation may be particularly appealing to the pediatric patient population. It is also appropriate for patients with renal impairment as it does not contribute to electrolyte imbalances (22). According to a review by Mulhem et al. (23) lactulose is recommended as a second-line treatment after polyethylene glycol for children with constipation. The European and North American Societies for pediatric gastroenterology, hepatology, and nutrition recommend lactulose as a first-line maintenance treatment for pediatric patients with chronic constipation if polyethylene glycol is not available (24).

Constipation is one of the most significant gastrointestinal complications in pregnant women (25). Li et al. (25) conducted a randomized controlled trial in 2020 on 113 pregnant patients with constipation, comparing the effects of taking 10 g of polyethylene glycol twice daily with 15 mL of lactulose twice daily. After a 3-week treatment period, no side effects were observed in either group, and both groups showed statistically and clinically significant improvements in Wexner constipation scores, with no significant difference found between the two groups (25).

Bisacodyl, while generally safe in most populations, should be used cautiously due to the potential risk of electrolyte imbalances, particularly in those with renal impairment or diuretics (4). It is contraindicated in pediatric patients under the age of 10 and has not been approved for use in pediatric patients by the FDA (20). Its safety during pregnancy has not been definitively established, and it should be used only when the potential benefits outweigh the risks (26).

Use in Inflammatory Bowel Disease (IBD) and Irritable Bowel Syndrome (IBS)

Both lactulose and bisacodyl may have roles in managing bowel-related symptoms in patients with IBD and IBS. However, they are not primary treatments for these conditions. Recent research suggests that restoring balance

to the gut microbiota could be a practical treatment approach in IBD and IBS (27). Prebiotics are indigestible food components that can stimulate the growth and activity of beneficial bacteria in the gut, and lactulose also has these prebiotic properties.

IBD: In patients with IBD, constipation can occur as a symptom, particularly in those with Crohn's disease affecting the colon or as a side effect of certain medications used to treat IBD. Lactulose has been used to manage constipation in IBD patients due to its mild osmotic action and good tolerance. It also has a potential role in reducing ammonia production, which can benefit patients with hepatic encephalopathy. This complication can occur in IBD patients with liver involvement. In addition to these effects, it has been found that lactulose as a prebiotic induces the growth of host microflora of a specific type that may help enhance the function of the gut. Furthermore, the demonstration that lactulose and other prebiotics have anti-inflammatory effects suggests potential additional benefits in managing diseases such as IBD (27). On the other hand, bisacodyl, due to its stimulant effect, should not be used as it may worsen IBD symptoms, particularly abdominal pain and diarrhea (20).

IBS: IBS is a functional bowel disorder characterized by chronic abdominal pain and altered bowel habits, including constipation (IBS-C), diarrhea (IBS-D), or both (IBS-M). In IBS-C, lactulose can soften stools and promote regular bowel movements. However, it may cause bloating and flatulence, which are often significant symptoms in IBS patients (28). Bisacodyl is also generally not recommended as a first-line treatment for IBS-C due to its potential to cause abdominal cramping. However, it may be used in patients who do not respond to other treatments (29).

Patient Compliance and Quality of Life

Patient compliance with treatment and the subsequent impact on quality of life are crucial considerations in managing constipation. Both lactulose and bisacodyl have unique characteristics that can influence these aspects.

Lactulose, due to its generally mild side effect profile and non-stimulant mechanism of action, may be better tolerated by some patients, promoting long-term compliance. In a study comparing lactulose with polyethylene glycol, both treatments were effective, but patient preference was significantly higher for lactulose due to its better taste (5). Another study on 112 children between 10 months and 15 years old showed that only two refused lactulose due to its taste (30). The fact that the side effects of lactulose, which

are mentioned in detail above, are milder and can be easily taken even by children contributes to patient compliance in long-term use.

With its faster onset of action, bisacodyl may be preferred by patients requiring rapid relief. However, the potential for abdominal cramping and electrolyte imbalances may limit its long-term use and patient compliance (4). Furthermore, the need for dose timing (usually recommended at bedtime to produce a morning bowel movement) may not suit all lifestyle patterns and could impact compliance (31).

In terms of quality of life, effective management of constipation can significantly improve patients' overall well-being and daily functioning (32). Given that lactulose and bisacodyl have demonstrated efficacy in relieving constipation, both can contribute positively to quality of life. However, the choice of laxative should consider individual patient factors such as tolerance of side effects, lifestyle, and personal preference to ensure optimal compliance and quality of life improvement.

Conclusion

The management of chronic constipation often requires long-term use of laxatives. Both lactulose and bisacodyl have shown efficacy in improving bowel movements and are widely used in clinical practice. However, lactulose might present a more favorable profile for certain patient populations when considering factors such as side effect profile, patient compliance, quality of life, and cost-effectiveness. Primary care physicians should consider these aspects when choosing the most appropriate treatment option for their patients, always considering individual patient characteristics and preferences.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.R.D., K.G., Concept: M.R.D., K.G., Design: M.R.D., K.G., Data Collection or Processing: M.R.D., K.G., Analysis or Interpretation: M.R.D., K.G., Literature Search: M.R.D., K.G., Writing: M.R.D., K.G.

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