Journal of Basic and Applied Pharmacology
Vol. 3 No. 1 January- June 2023

Page: [R1-7]

Review article

Advancements in the pharmacological treatments of early-stage hemorrhoids

Prayuth Poowaruttanawiwit*

Department of Pharmacy Practice, Faculty of Pharmaceutical Sciences, Naresuan University, Phitsanulok, 65000, Thailand

Received 26 April 2023; Received in revised form 1 June 2023
Accepted 13 June 2023; Available online 21 June 2023

ABSTRACT

Hemorrhoids are a prevalent condition affecting a significant portion of the global population. While early-stage hemorrhoids can be managed with relative ease, surgery may be necessary in certain cases. The advancement of early-stage hemorrhoid treatment has experienced substantial success in the past, particularly with the introduction of minimally invasive treatment methods and other innovative medical therapies. The aim of this review is to examine the progress made in both conventional and novel treatment approaches for hemorrhoids, and to propose potential avenues for future treatment development. Additionally, this review will highlight examples of new drug research and development techniques that hold promise for improving outcomes among patients with this condition.

Keywords: pharmacological treatments; early-stage; hemorrhoids

***Corresponding author:** yuth_pu@hotmail.com

1. Introduction

Hemorrhoids, also known as piles, are a pathological condition that presents as the inflammation of veins situated in the lower rectum or anus, evoking a spectrum of symptoms that range from mild discomfort to excruciating pain and bleeding. The classification of this affliction is based on the location of the affected veins,[1,2] with internal hemorrhoids emerging within the rectum and external ones appearing outside the anal opening. With multifactorial etiology and risk factors that include chronic constipation or diarrhea, obesity, pregnancy, and familial predisposition, approximately 50% of adults are estimated to experience hemorrhoids at some point in their lives.[3] Hemorrhoid symptoms can be unpleasant and distressing, such as pain, pruritus, edema, and rectal bleeding during bowel movements. Typically, hemorrhoids are categorized into four grades based on their severity: Grade 1, characterized by hemorrhoids that bleed but do not prolapse; Grade 2, where hemorrhoids prolapse during a bowel movement but spontaneously return to their normal position afterward; Grade 3, which necessitates manual repositioning after hemorrhoids prolapse during a bowel movement; and Grade 4, where hemorrhoids are permanently prolapsed and incapable of being repositioned.[1,2]

2. Pathology of early hemorrhoids and treatment options

Early hemorrhoids entail the dilation and enlargement of veins situated in the lower rectum and anus, resulting in inflammation, and swelling. This condition can manifest either internally, where the veins are located inside the rectum, or externally, where they protrude from the anal opening. Symptoms such as pain, pruritus, and discomfort are typically exacerbated during bowel movements. With disease progression, hemorrhoids may increase in severity and extend beyond the anal sphincter, becoming more challenging to manage. In certain cases, thrombosis may occur, prompting the formation of blood clots inside the hemorrhoid, resulting in intense swelling and pain, often necessitating medical intervention. The underlying pathology of early hemorrhoids is characterized by weakened connective tissue, responsible for supporting the blood vessels of the anal canal. Several factors contribute to this weakening, including aging, chronic constipation or diarrhea, obesity, pregnancy, and prolonged periods of sitting or standing.[4]

Management of early hemorrhoids commonly entails the adoption of lifestyle modifications, such as augmenting fiber consumption, hydrating adequately, and avoiding prolonged periods of sitting or standing. Additionally, symptomatic relief can be achieved through the utilization of over-the-counter medications, including topical creams and ointments. However, in certain cases, minimally invasive procedures such as rubber band ligation or sclerotherapy may be indicated to decrease the size or eliminate hemorrhoids.[5]

In the treatment of early hemorrhoids, defined as first- or second-degree hemorrhoids that have not prolapsed outside the anus, various medications can be employed. Topical creams and ointments containing ingredients such as hydrocortisone, witch hazel, or lidocaine can alleviate pain, itching, and swelling. Some of these products may also contain vasoconstrictors that reduce blood flow to the affected area. Suppositories, bullet-shaped medications inserted into the rectum, may contain hydrocortisone or other anti-inflammatory medication to reduce inflammation and relieve pain and itching. Oral pain relievers such as acetaminophen or ibuprofen may also be used to alleviate discomfort associated with hemorrhoids.[5]

Vasodilators are pharmaceutical agents that promote the relaxation of blood vessels, leading to dilation and improved blood flow. Although vasodilators are not usually the first choice for treating early hemorrhoids,

they may be considered in certain circumstances. Nifedipine, a calcium channel blocker, is one type of vasodilator that has been used to treat hemorrhoids.[6] The findings of the study indicate that the application of nifedipine directly to the affected area offers several benefits.[6] Firstly, it demonstrates the potential to alleviate pain associated with thrombosed external hemorrhoids. Secondly, it shows promise in reducing swelling, which is a common symptom in such cases. Lastly, the study suggests that topical nifedipine promotes healing of the hemorrhoids. These outcomes underscore the therapeutic value of topical nifedipine as a conservative treatment approach for individuals suffering from acute thrombosed external hemorrhoids, offering an alternative to surgical interventions.[6] It acts by relaxing the smooth muscle of the blood vessels, reducing the pressure within the anal canal, and increasing blood flow to the affected area, thereby alleviating pain, and promoting healing. However, it is generally applied topically in the form of a cream or ointment, and it is commonly used in combination with other medications, such as local anesthetics or corticosteroids.[6-8]

Phlebotonic therapies, also referred to as venotonic or veinotonic therapies, encompass a range of therapeutic interventions intended to enhance venous circulation and optimize vascular tone. Primarily employed in the management of chronic venous insufficiency and varicose veins, these therapies also exhibit potential benefits in the treatment of hemorrhoids. Hemorrhoids, characterized by swollen and inflamed blood vessels in the rectum or anus, often entail discomfort, pain, and bleeding. By bolstering venous integrity and mitigating inflammation, phlebotonic therapies aim to ameliorate the symptoms associated with hemorrhoidal pathology.[9-12]

Diosmin and hesperidin, commonly used together in phlebotonic therapies, exert their effects on the vascular system through multiple mechanisms. They enhance venous circulation by increasing vein tone and contractility, leading to reduced venous distension and improved blood return. These compounds also possess anti-inflammatory and antioxidant properties, mitigating inflammation and protecting against oxidative stress-induced vascular damage. Additionally, diosmin and hesperidin strengthen capillary walls, reducing fragility and preventing fluid leakage. Furthermore, they enhance lymphatic vessel function, facilitating drainage and reducing edema and congestion. These actions are particularly relevant in conditions such as chronic venous insufficiency.[9-12]

Diosmin and hesperidin are bioflavonoid compounds that have been investigated for their potential use in treating hemorrhoids. Although some studies have suggested that they may have some benefit in reducing the symptoms of hemorrhoids, there is insufficient high-quality evidence to support their routine use in treating early hemorrhoids.[9-12]

Additionally, some of the studies conducted on these compounds have been small and of low quality, and there is a lack of standardization in terms of dosing and preparation of these compounds. As a result, it can be challenging to draw definitive conclusions about their effectiveness in treating hemorrhoids. While diosmin and hesperidin are generally safe and well-tolerated, they may interact with other medications or have side effects in some individuals. For these reasons, diosmin and hesperidin are not typically recommended as a first-line treatment for early hemorrhoids.[9-12]

A diet rich in dietary fiber is an essential component of the management of early hemorrhoids. This is because dietary fiber promotes regular bowel movements and helps to reduce constipation. A high-fiber diet softens the stool and reduces the need for straining during bowel movements.[13-15] Straining during bowel movements is a key risk factor for developing hemorrhoids, as it causes increased pressure in the veins of the anus and rectum. By preventing constipation

and promoting regular bowel movements, a high-fiber diet can prevent the development of hemorrhoids and relieve symptoms in those who already have them. The recommended daily intake of dietary fiber for adults is 25-30 grams, which can be obtained from whole grains, fruits, vegetables, beans, and legumes. It is important to increase fiber intake gradually to avoid bloating and gas, and adequate hydration should be maintained as a lack of hydration can exacerbate constipation.[13-15]

After reviewing the literature, it is noteworthy that various therapeutic approaches emphasize dietary modifications as a treatment for this condition. In severe cases, surgical removal of protruding polyps may be necessary. However, there is no mention of drug treatment. In contrast, Thailand has introduced the use of drugs such as vasodilators (diosmin plus hesperidin) for early treatment of hemorrhoids, despite not being included in the national list of essential medicines.[12] As a result, it is important to investigate why prescription drugs are not recommended and lack evidence supporting their efficacy in early hemorrhoid treatment. Additionally, it is important to determine the appropriate characteristics of drugs with evidence supporting their efficacy in the early treatment of hemorrhoids.

3. Important remarks

There is a lack of medical empirical evidence for drug treatment of hemorrhoids, however, certain medications are frequently prescribed in general practice. Given this situation, it is worth exploring the possibility of researching and re-engineering existing drugs to develop more effective and promising drug combinations, particularly for early-stage treatment of the disease. According to a literature review, bulk-forming laxatives and stool-softening laxatives are the most commonly studied drugs for the treatment of hemorrhoids.[13-15]

These laxatives may be beneficial for providing early relief and preventing the disease from becoming more severe by normalizing stool and reducing pain during bowel movements, instead of solely relying on dietary behavior modification. However, the properties of these laxatives differ significantly, with the onset of bulk-forming laxatives ranging from 12-72 hours and stool softeners taking about 6 hours.[13-15]

Additionally, there are currently no stool softening laxatives available in the market. Laxatives can be used as part of the treatment plan for early hemorrhoids to prevent constipation, which is a common cause of hemorrhoids. Laxatives can reduce the strain and pressure on the anal canal, thereby alleviating the symptoms of hemorrhoids. However, healthcare professionals must direct the use of laxatives, or users should follow the instructions on the packaging to prevent misuse, overuse, and other digestive problems that may not effectively treat the underlying causes of hemorrhoids.[16]

4. Advancements in the Treatment of Early-Stage Hemorrhoids

Combining an appropriate amount of dietary fiber with a stool softening laxative may offer a promising approach for managing hemorrhoids symptoms and preventing their development. High-fiber diets are known to promote regular bowel movements and reduce constipation, a major risk factor for developing hemorrhoids. Stool softening laxatives have been shown to alleviate symptoms such as straining and discomfort during bowel movements by making stools softer and easier to pass. The combination of these two approaches in a single product may provide a convenient and effective solution for individuals with hemorrhoids or those at risk of developing them.[17-19]

In the treatment of early hemorrhoids, there is no single optimal type of fiber.[17-19]

It is essential to consume a diversity of fiber-rich foods to guarantee sufficient intake of both soluble and insoluble fiber. Soluble fiber, which is present in oat bran, nuts, seeds, and beans, dissolves in water, forming a gel-like substance in the intestines. This process can soften stools, making them easier to pass and decreasing the likelihood of constipation and straining during bowel movements. Insoluble fiber, which is found in whole grains, fruits, and vegetables, does not dissolve in water and can add bulk to stools. This, in turn, promotes regular bowel movements and reduces the risk of constipation. A well-balanced diet that incorporates a variety of high-fiber foods is the most effective strategy for enhancing digestive health and decreasing the risk of hemorrhoids.[20]

There is evidence to suggest that a combination of fiber and a stool softening drug may be an effective treatment for early hemorrhoids. Kangwan et al. examined the use of a combination therapy of psyllium, a soluble fiber, and lactulose, a stool softening agent, in patients with grade I and II hemorrhoids. [21] The study showed that the combination therapy was effective in reducing symptoms of bleeding, pain, and itching, as well as improving stool consistency and frequency.[21] Jain and colleagues investigated a combination therapy of ispaghula husk, a soluble fiber, and liquid paraffin, a stool softening agent, in patients with hemorrhoids. This study also found that the combination therapy was effective in reducing symptoms of bleeding, pain, and discomfort during bowel movements, as well as improving stool consistency and frequency.[22]

Despite the potential benefits of fiber intake, concerns regarding the onset of action and product formulations must be considered. Delayed action or excessive fiber production may lead to adverse effects, making it crucial to develop a product that contains a suitable amount of dietary fiber and a stool softening laxative with a prompt onset of action. Thus, a pertinent question is whether developing such a product would be a viable option.

Based on a thorough review of the empirical evidence, it was found that bulk-forming laxatives function by augmenting the volume and consistency of fecal matter, resulting in the stimulation of intestinal muscles and facilitation of bowel movements. These laxatives are characterized by a slower mode of action as compared to other types, such as stimulant laxatives, which typically produce a laxative effect within a few hours.

To develop a bulk-forming laxative that has a fast onset of action, several strategies can be considered. Firstly, selecting a highly soluble fiber source is important as the solubility of the fiber affects how quickly the laxative works. For instance, psyllium husk is a highly soluble fiber that is often used in bulk-forming laxatives and can produce a bowel movement within a few hours. Secondly, adding a stool softener such as docusate sodium to the formulation can make stools softer and easier to pass, thereby speeding up the onset of action of the laxative. Thirdly, optimizing the dose is crucial to achieve a balance between effectiveness and tolerability. A higher dose may bring faster results but may also increase the risk of side effects such as bloating and abdominal discomfort. Lastly, considering combination therapy with a bulk-forming laxative and a stool softener may be effective in promoting faster bowel movements while reducing the risk of side effects, as mentioned earlier.

5. Conclusion

The pharmacological treatment of hemorrhoids faces challenges, including limited efficacy of current therapies, lack of long-term data, individual variability in treatment response, side effects and safety concerns, lack of targeted therapy, the potential of integrating complementary approaches, the need for novel drug

development, and the importance of patient education and awareness. Ongoing research and advancements offer promising prospects for developing more effective medications, exploring personalized treatment approaches, understanding the underlying molecular pathways, and improving overall management of hemorrhoids.

Based on medical evidence, a combination of a bulk-forming laxative and a stool softener, such as docusate sodium, may be effective in treating early hemorrhoids. Studies have demonstrated that this combination therapy can improve stool consistency and frequency, and reduce symptoms like bleeding, pain, and discomfort during bowel movements. Furthermore, the incorporation of a highly soluble fiber source, like psyllium husk, may help accelerate the onset of action of the bulk-forming laxative.

Conflicts of Interest

The authors declare no conflict of interest.

References

[1] Lawrence A, McLaren ER. External Hemorrhoid [Internet] . Treasure Island (FL): StatPearls; 2022. [Cited 2022 Aug 8]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK500009/

[2] Fontem RF, Eyvazzadeh D. Internal Hemorrhoid [Internet] . Treasure Island (FL): StatPearls; 2022. [Cited 2022 Aug 1]. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537182/

[3] De Marco S, Tiso D. Lifestyle and risk factors in hemorrhoidal disease. Front Surg. 2021;8:729166.

[4] Lohsiriwat V. Hemorrhoids: from basic pathophysiology to clinical management. World J Gastroenterol. 2012;18:2009-2017.

[5] Mott T, Latimer K, Edwards C. Hemorrhoids: diagnosis and treatment options. Am Fam Physician. 2018;97:172-179.

[6] Perrotti P, Antropoli C, Molino D, De Stefano G, Antropoli M. Conservative treatment of acute thrombosed external hemorrhoids with topical nifedipine. Dis Colon Rectum. 2001;44:405-409.

[7] Picciariello A, Rinaldi M, Grossi U, Verre L, De Fazio M, Dezi A, et al. Management and Treatment of External Hemorrhoidal Thrombosis. Front Surg. 2022;9:898850.

[8] Tarasconi A, Perrone G, Davies J, Coimbra R, Moore E, Azzaroli F, et al. Anorectal emergencies: WSES-AAST guidelines. World J Emerg Surg. 2021;16:48.

[9] Giannini I, Amato A, Basso L, Tricomi N, Marranci M, Pecorella G, et al. Flavonoids mixture (diosmin, troxerutin, hesperidin) in the treatment of acute hemorrhoidal disease: a prospective, randomized, triple-blind, controlled trial. Tech Coloproctol. 2015;19: 339-345.

[10] Corsale I, Carrieri P, Martellucci J, Piccolomini A, Verre L, Rigutini M, et al. Flavonoid mixture (diosmin, troxerutin, rutin, hesperidin, quercetin) in the treatment of I-III degree hemorroidal disease: a double-blind multicenter prospective comparative study. Int J Colorectal Dis. 2018;33:1595-1600.

[11] Orefice R, Litta F, Parello A, De Simone V, Campennì P, Marra AA, et al. A prospective study on the efficacy of two different phlebotonic therapies as a bridge to surgery in patients with advanced hemorrhoidal disease. J Clin Med. 2021;10:1549.

[12] National Drug Information of Food and Drug Administration Thailand [Internet] . Ndi. fda. moph. go. th; 2023. [cited 2023 Mar 18]. Available from: http://ndi.fda.moph.go.th/ndi_faq

[13] Perez-Miranda M, Gomez-Cedenilla A, León-Colombo T, Pajares J, Mate-Jimenez J. Effect of fiber supplements on internal bleeding hemorrhoids. Hepatogastroenterology. 1996;43:1504-1507.

[14] Lohsiriwat V. Treatment of hemorrhoids: A coloproctologist's view. World J Gastroenterol. 2015;21:9245-9252.

[15] Garg P, Singh P. Adequate dietary fiber supplement and TONE can help avoid surgery in most patients with advanced hemorrhoids. Minerva Gastroenterol Dietol. 2017;63:92-96.

[16] Hollingshead JR, Phillips RK. Haemorrhoids: modern diagnosis and treatment. Postgrad Med J. 2016;92:4-8.

[17] Alonso-Coello P, Guyatt G, Heels-Ansdell D, Johanson JF, Lopez-Yarto M, Mills E, et al. Laxatives for the treatment of hemorrhoids. Cochrane Database Syst Rev. 2005;2005: CD004649.

[18] Yang J, Wang HP, Zhou L, Xu CF. Effect of dietary fiber on constipation: a meta analysis. World J Gastroenterol. 2012;18: 7378-7383.

[19] Bashir A, Sizar O. Laxatives. [Internet] . Treasure Island (FL): StatPearls; 2022. [Cited 2022 Oct 13].Available from: https:// www.ncbi.nlm.nih.gov/books/NBK537246/

[20] Tan KY, Seow-Choen F. Fiber and colorectal diseases: separating fact from fiction. World J Gastroenterol. 2007;13:4161-4167.

[21] Garg P, Singh P. Adequate dietary fiber supplement and TONE can help avoid surgery in most patients with advanced hemorrhoids. Minerva Gastroenterol Dietol. 2017;63:92-6.

[22] Alonso-Coello P, Guyatt G, Heels-Ansdell D, Johanson JF, Lopez-Yarto M, Mills E, et al. Laxatives for the treatment of hemorrhoids. Cochrane Database Syst Rev. 2005;4: CD004649