Understanding Hemorrhoids and its Management

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Hemorrhoids: An overview

Hemorrhoids is defined as the symptomatic enlargement and/or distal displacement of anal cushions, which are prominences of anal mucosa formed by loose connective tissue, smooth muscle, arterial and venous vessels.[1] In India, it is one of the most common anorectal diseases that various general practitioners, general surgeons, and gastrointestinal surgeons come across in their daily practice.[2] Although, it is speculated that about 50% of the population would have encountered hemorrhoids at some point in their life, the peak incidence of this condition appears to occur between the ages of 45-65 years. It is unusual to develop hemorrhoids before 20 years of age, and the risk is higher for whites than for blacks. Also, there is an increased risk of hemorrhoids associated with pregnancy, and an increased prevalence, in general, in females compared to males.[3]

Pathophysiology of hemorrhoids

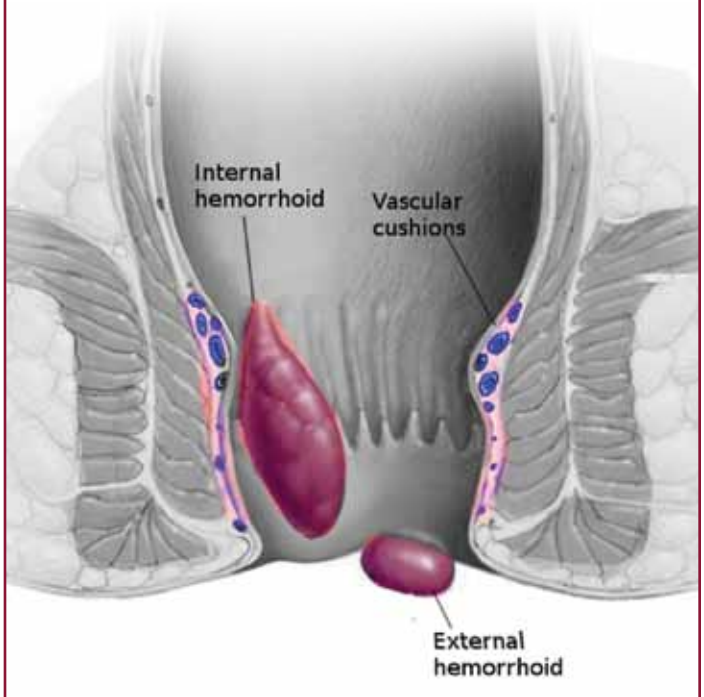
The exact pathophysiology of development of hemorrhoids is not understood clearly.[1] Several etiological factors have been associated with the development of hemorrhoids, including chronic straining while defecation, inadequate dietary fiber intake, constipation, diarrhea, pregnancy, sedentary lifestyle, and familial predisposition. It is believed that all these factors play a role in the development of hemorrhoidal disease in individual patients.[3]

Although various theories have been hypothesized, the most commonly accepted hypothesis is sliding of the anal canal lining. Basically, there are three major anal cushions, located in the right anterior, right posterior and left lateral aspect of the anal canal, along with numerous minor cushions lying between them. This hypothesis proposes that hemorrhoids develop when disintegration or deterioration of the supporting tissues of the anal cushions occurs due to which there is abnormal downward displacement of the anal cushions causing venous dilatation. These anal cushions of patients with hemorrhoids demonstrate significant pathological changes along with venous dilatation, including, vascular thrombosis, degenerative process in the collagen fibers and fibroelastic tissues, and distortion and rupture of the anal subepithelial muscle. Additionally, specimen from hemorrhoidal tissue demonstrate a severe inflammatory reaction involving the vascular wall and surrounding connective tissue with mucosal ulceration, ischemia and thrombosis.[1]

Classification of hemorrhoids

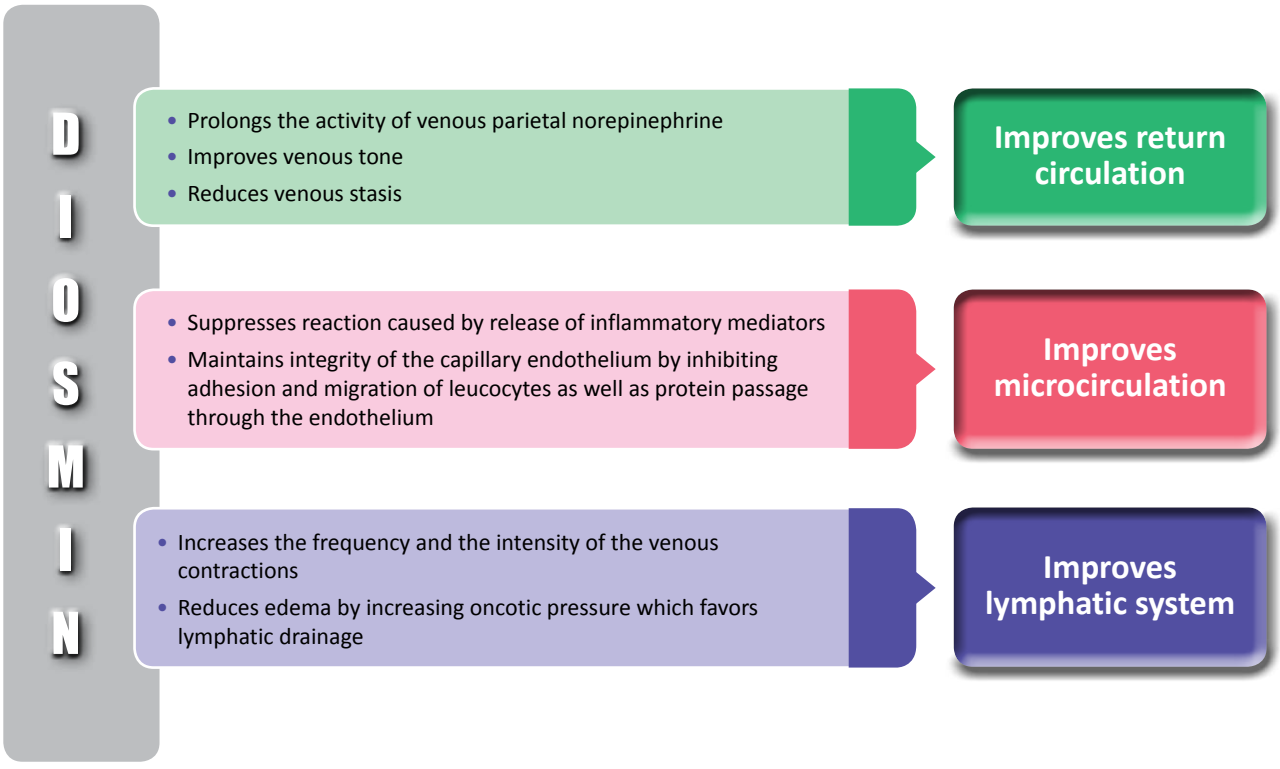
Classification of hemorrhoids is done on the basis of their location and degree of prolapsed. Origin of internal hemorrhoids is from the inferior hemorrhoidal venous plexus above the dentate line and these are covered by mucosa, while external hemorrhoids are dilated venules of this plexus located below the dentate line and are covered with squamous epithelium (Figure 1). Mixed (interno-external) hemorrhoids arise both above and below the dentate line.[1,3,4] Internal hemorrhoids are further divided into four grades according to Goligher's classification (Table 1).[5]

Figure 1: Classification of haemorrhoids



Adapted from: Fontem RF, Bhimji SS. Internal Hemorrhoid. [Updated 2019 Feb 2]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2019 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK537182/ Acessed on: 28.3.2019.

Figure 2: Multiple mechanisms of action of Diosmin



Abbreviation: COMT; Catechol-O-methyltransferase

Adapted from: Steinbruch M, Geller M, Kaufman R, Rzetelna H, Nunes CP, *et al.* Use of Pure Diosmin 600 mg in Chronic Venous Disease: A Review of the Literature. *RBM.* 2015;72(7):307-314.

Table 1: Grades of internal hemorrhoids

First Degree/Grade 1	Anal cushions bleed but do not prolapse	
Second degree/Grade 2	Anal cushions prolapsed through the anus on straining	But reduce spontaneously
Third degree/Grade 3		But require manual replacement into the anal canal
Fourth degree/Grade 4		Is irreducible

Adapted from: Vagholkar K, Chawathey S, Shekhar S, Vagholkar S. Hemorrhoids: Which is the best therapeutic option? *Int Surg J.* 2018;5(8):2689-2692.

Clinical evaluation

According to the American Society of Colon and Rectal Surgeons (ASCRS) clinical practice guidelines 2018, management of hemorrhoids should begin with a disease-specific history and physical examination, with an emphasis on the severity and duration of symptoms and risk factors. The physical examination in the prone, knee-chest, or lateral decubitus position should include visual inspection of the anus along with a digital rectal examination to assess for other anal pathology and integrity of the sphincter. In addition, in some patients with symptomatic hemorrhoids and rectal bleeding, complete endoscopic evaluation of the colon is indicated (Box 1).[6]

Box 1: Indications for complete colon evaluation

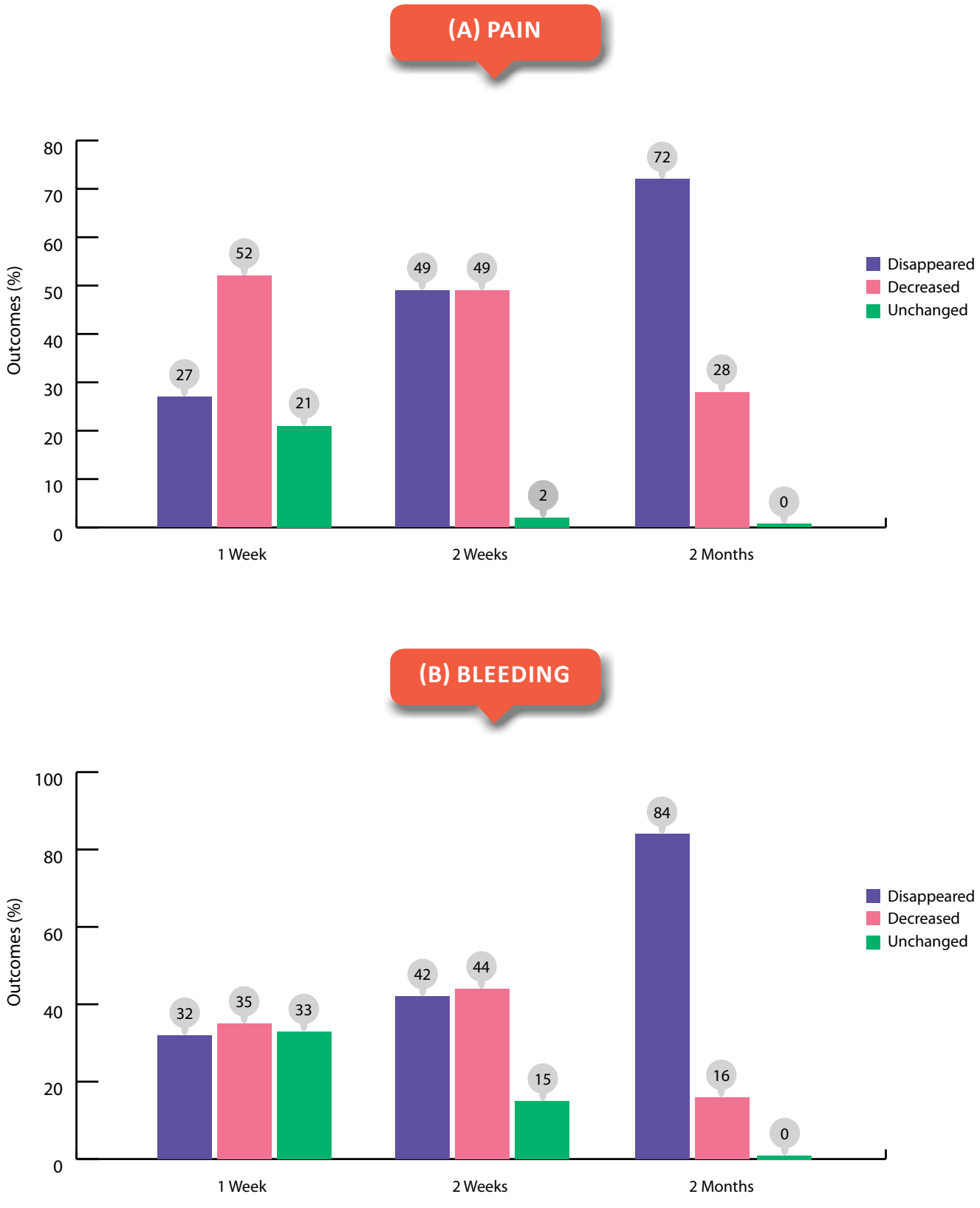
- Age ≥50 years if no complete examination within 10 years
- Age ≥40 years or 10 years younger than the age at diagnosis with history positive for a single, first-degree relative with colorectal cancer or advanced adenoma diagnosed at age <60 years
- Age ≥40 years or 10 years younger than the age at diagnosis with history positive for two first-degree relatives with advanced adenomas or colorectal cancer
- Positive fecal immunochemical testing (FIT)
- Positive FIT-fecal DNA test.

Adapted from: Davis BR, Lee-Kong SA, Migaly J, Feingold DL, Steele SR. The American Society of Colon and Rectal Surgeons Clinical Practice Guidelines for the Management of Hemorrhoids. *Dis Colon Rectum.* 2018;61:284–292.

Management of hemorrhoids: A focus on medical therapy

Early stages of hemorrhoids can be managed with conservative approaches that include lifestyle modifications, fibre supplementation, use of topical ointments, and use of

Figure 3: Improvement in (A) pain and (B) bleeding with use of diosmin in patients with hemorrhoids



Adapted from: Diana G, Catanzaro M, Ferrara A, Ferrari P. Activity of Diosmine pure in the treatment of Haemorrhoidal disease. *Clin Ter.* 2000;151: 341-344.

phlebotomic drugs. Advanced stages of the disease (III/IV degree) require surgical interventions; however, medical therapy is still useful to minimize anal symptoms of edema and inflammation as a bridge-to-treatment.[7,8]

Phlebotonics are a heterogenous class of drugs used for the management of acute as well as chronic cases of hemorrhoids. Even though a true mechanism of action of these drugs has not been ascertained, they have been found to strengthen blood vessels, increase venous tone and lymphatic drainage, and normalize capillary permeability.[6] In a Cochrane review,[9] involving 2334 participants [24 randomized controlled trials (RCTs)], phlebotonics were compared with a control in improving the signs, symptoms and severity of hemorrhoids. It was found that use of phlebotonics was associated with significant beneficial effects, with improvement in outcomes of pruritus, bleeding, discharge, leakage, and overall symptom improvement.[9]

Flavonoids such are the most commonly used phlebotonic agents in management of hemorrhoids. It is believed that flavonoids have the capability to increase vascular tone, reduce venous capacity, decrease capillary permeability, and facilitate lymphatic drainage.[1] In addition; these also exhibit vasculoprotective effects and are antagonistic to biochemical mediators of inflammation.[10] In a meta analysis[11] comparing flavonoids (Diosmin, micronized purified flavonoid fraction, and rutosides) with placebo or no treatment in patients (*n*=1514) having symptomatic hemorrhoids, flavonoid therapy demonstrated a reduction in the risk of bleeding, persistent pain, itching and recurrence.[11]

Appraising the therapeutic utility of Diosmin

Diosmin is an oral phlebotonic drug that is commonly used for the management of hemorrhoids.[8] It has been noted that Diosmin achieves maximum plasma concentration after about one hour of administration, with a half life of 26-43 hours.[12,13] Diosmin acts by targeting multiple pathophysiological aspects of hemorrhoids, thus, aiding in amelioration of the associated disease symptoms as well (Figure 2).[14]

An important consideration while treating patients with Diosmin is selection of the pure form of Diosmin. Several variants of the Diosmin preparation contain various impurities, such as hesperidin, linarin, and isorhoifolin, which can interfere with clinical efficacy of the preparation.[15,16] Hesperidin has also been regarded as impurity B by the British Pharmacopoeia.[17] Several evidences support the superior clinical efficacy of pure Diosmin in the management of hemorrhoids. In one such study,[8] use of purified Diosmin at a dose of two 450 mg tablets for 7 days followed by one tablet bid for upto two months in patients (*n*=66) having primitive hemorrhoids of grade 1-4, demonstrated that Diosmin was efficient in decreasing pain as well as bleeding (Figure 3). Reduction rates for pain were 79% in the first treatment week and 98% in the second week, while for bleeding these were 67% and 86%, respectively. Additionally, Diosmin displayed a good tolerability.[8]

Conclusion

Overall, the above discussion clearly shows that Diosmin is an ideal treatment for hemorrhoids when in its 100% pure form as a monosubstance. In all, the efficacy of Diosmin is well established in attenuating and treating the symptoms of hemorrhoids.

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