

Treatment of haemorrhoids in pregnancy:

A retrospective review



Ann. Ital. Chir., 2023 94, 3: 274-280
pii: S0003469X23038745

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AIM: Haemorrhoids are varicose veins of the rectum covered by mucosa at or near the anal canal. They are normally asymptomatic, can occur at any age and affect both males and females. Haemorrhoids are common in young women and commoner during pregnancy and the puerperium. In this review, we address the issue of the approach of the obstetrician and surgeons to haemorrhoids and their management. This is significant because there are currently no recommendations for pregnant patients with hemorrhoids.

METHODS: The literature search comprised all the inherent published original papers; also abstract were included. No language selection was done. Search terms used were: "hemorrhoid", "hemorrhoid therapy", "hemorrhoid in pregnancy", "hemorrhoid complication". Data research was conducted using MEDLINE, EMBASE, Web of Sciences, Scopus, Clinical Trial. gov, OVID and Cochrane Library querying for all articles related to treatment of hemorrhoidis in pregnancy.

RESULTS: Fiber supplement, stool softener and mild laxatives are generally safe for pregnant women. Topical medication or oral phlebotonics may be used with special caution because the strong evidence of their safety and efficacy in pregnancy is lacking. In case of massive bleeding, anal packing could be a simple and useful maneuver. Hemorrhoidectomy is reserved in strangulated or extensively thrombosed hemorrhoids, and hemorrhoids with intractable bleeding.

KEY WORDS: Hemorrhoid, Hemorrhoid Therapy, Hemorrhoid in Pregnancy, Hemorrhoid Complication

Introduction

Hemorrhoids are one of the most prevalent diseases in Western countries. It is reported an incidence ranging between 58 and 86 % and a prevalence between 5 and 35%. The onset before 20 years of age is quite unusual, while the higher incidence peaks occur between 45 and 65 years of age ¹. Hemorrhoids affect 25-35% of pregnant women, with peaks of 85% in some ethnic

groups. Hemorrhoids appear especially in the third trimester and could be both internal and external. The probability of developing venous insufficiency is 34% in the first pregnancy, 60 % in the second up to 70% in the third pregnancy ².

At the beginning of the 6th week of pregnancy there is an increase in blood volume (40-50% of the volume before the pregnancy) caused by estrogen and progesterone, that increase plasma volume by reducing the release of proteins from the endothelial bed. Besides there is a widening of the vascular bed, especially at the utero-placental circulation and in the mammary glands. There is also an increase of the cardiac output, that reaches the maximum in 24 weeks; all of these effects cause an enlarged flow in utero-placental vessels and causes an effect that can be compared to an arteriovenous fistula, raising the inflow and the pressure in the pelvic veins

Pervenuto in Redazione Agosto 2022. Accettato per la pubblicazione Ottobre 2022

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and a concurrent decrease in blood flow to the lower extremities^{3,4}. Those mechanisms cause a raised flow in collateral circulatory veins (vulvar, rectal, and lumbar), with an higher risk of developing varicose veins, hemorrhoids and teleangectasia. The swelled uterus during pregnancy compresses the pelvis veins with obstruction of the outflow from the lower extremities⁵. Venous relaxation is caused by a rise in venous pressure combined with hormonal changes occurring in the first trimester of pregnancy. A number of mediators (progesterone, estrogens, prostaglandins, cyclic adenosine monophosphate (cAMP) and intracellular calcium exchange) effecting the vascular wall level, have been identified^{5,6}. Estrogens are responsible for mesenchymal release, while progesterone is responsible for a generalized myolytic effect. These effects on the venous system cause a tissue vascular dislocation (estrogen) and a reduction in venous tone (progesterone).

The progesterone receptor can be particularly found in the safenic site, which is located on the smooth muscle cells of the tunica media and in the subendothelial layer^{7,8}; this explains the easy appearance of venous dilations during pregnancy. Varicose veins have been most commonly found in women with a higher concentration of progesterone in serum. In non-pregnant women, this level varies from less than 1 nmol / L to 20 nmol / L depending on the stage of the cycle, and is greater in the luteal phase⁷⁻¹⁰.

Some conditions (e.g. constipation and prolonged efforts) cause an increase in intra-abdominal pressure, and could help in the development of hemorrhoids as a result of altered venous drainage through the hemorrhoid plexus¹⁰. Some types of food and lifestyle, including diet poor of fibers, spicy foods and alcohol intake, could play a role in the development of hemorrhoids and the aggravation of symptoms¹¹.

The most common presentation of hemorrhoidal pathology is rectal bleeding during defecation without pain, with or without prolapse of anal tissue. Blood normally covers the outer surface of the stools, or is found directly at the time of cleansing. Blood is typically brilliant red due to direct arteriovenous communication in the hemorrhoidal plexus¹². Patients with complicated hemorrhoids such as external hemorrhoids with thrombosis or internal incarcerated hemorrhoids may have anal pain. In clinical examination it may be detected a nodule at the level of the anal margin.

Anal pain in patients with uncomplicated hemorrhoids is not common. In fact anal pain in patients with hemorrhoids is more likely to be related to the presence of anal fissure or anal abscess¹³. Accurate history and objective examination, including digital rectal examination and anoscopy, are crucial for the diagnosis of hemorrhoids. Hemorrhoids are generally classified by their location; internal (originates above the dentate line and covered by anal mucosa), external (originates below the dentate line and covered by anoderm) and mixed type. Internal

hemorrhoids are further graded based on their appearance and degree of prolapse:

- Grade I: non-prolapsing hemorrhoids;
- Grade II: prolapsing hemorrhoids on straining but reduce spontaneously;
- Grade III: prolapsing hemorrhoids requiring manual reduction;
- Grade IV: non reducible prolapsing hemorrhoids which include acutely thrombosed, incarcerated hemorrhoids¹⁴.

Materials and Methods

Here, we present and discuss the approach of the obstetrician and surgeons to haemorrhoids and their management. No language selection was done. Search terms used were: “hemorrhoid”, “hemorrhoid therapy”, “hemorrhoid in pregnancy”, “hemorrhoid complication”. Data research was conducted using MEDLINE, EMBASE, Web of Sciences, Scopus, ClinicalTrial.gov, OVID and Cochrane Library querying for all articles related to treatment of hemorrhoids in pregnancy. If there were any missing data, the corresponding authors of the articles in question were contacted by email. Articles containing adequate information, such as publication year, patient age, sex, duration of complaint, therapy, were included, while studies and comment articles with insufficient clinical and demographic data were excluded.

Discussion

The aim of hemorrhoids treatment in pregnant women is to control the symptoms, which often resolve spontaneously in the puerperium, and the protection of the perineal region, exposed to trauma during vaginal delivery. A conservative approach is always recommended, except when acute thrombosis occurs. Any surgical treatment should be postponed, if possible, a few weeks after delivery.

In 2010 Avsar wrote “The Best Treatment of Prevention” to highlight the role of proper nutrition with proper fiber and fluid intake in positively affecting constipation, which is one of the factors contributing to the onset of hemorrhoids in pregnancy. During pregnancy, physiological changes such as compression of the lower intestine by the pregnant uterus are observed, resulting in mechanical obstruction, reduced intestinal transit, smooth muscle relaxation and increased colonic liquid absorption, which lead to changes in intestinal regularity and often hesitate in constipation.

Constipation is therefore an important factor for the onset of hemorrhoids in pregnancy and the modification of the food plan is indeed the first treatment for this pathology. Regular consumption of fresh fruit and vegetables and an adequate supply of water are recommended¹⁵. A study evaluating fibers increasing for two

weeks (in the form of wheat bran) in 40 women in the third trimester of pregnancy, showed a significant increase in intestinal motility in those who had taken 10g of fiber in the form of biscuits or wheat bran compared to the control group¹⁶.

Moderate physical exercise improves intestinal motility and supports anorectal coordination and should be counted among the hygienic measures to be taken during pregnancy.

Natural laxatives such as Psyllium act as mass formative laxatives that draw water into the intestinal lumen and accelerate transit time. A broad trial has shown Psyllium superiority to placebo in terms of frequency and consistency of stools¹⁷. In the treatment of constipation, the use of Psyllium has been associated with increased intestinal transit and intestinal motility and the production of soft and well lubricated stool¹⁸.

Osmotic laxatives contain non-reassorbable ions or molecules that retain water in the intestinal lumen. The most commonly used are polyethylene glycol (PEG) and lactulose. Based on the results of a meta-analysis, polyethylene glycol (PEG) has been shown to be more effective than lactulose in terms of frequency and consistency of stools, with lesser adverse reactions; osmotic laxatives should be therefore considered as the first choice¹⁹. In addition, the good safety and tolerability profile makes them available in special situations such as pregnancy. Safety of stimulant laxatives during pregnancy, including diphenylmethane (eg bisaculide, sodium picosulphate) and anthraquinones (eg, sand), is not enough demonstrated and their use is currently discouraged. Even spasmolytic drugs such as calcium antagonists (otilonium, pinaverio), muscle relaxant drugs (mebeverine), antimuscarinic / anticholinergic drugs (scopolamine, cimetrop, dicyclonine), serotonergic agonists (prucalopride), cyclase C guanilate agonists (linaclotide), lubiprostone (derived prostaglandin) are not currently recommended for no strong evidences of their safety profiles have been provided yet. There is no evidence regarding the use of peppermint essence (with spasmolytic activity)²⁰. Mineral oils (vaseline oil) with emollient action do not appear to be associated with adverse reactions; their continued use is related to the reduction in the maternal absorption of liposoluble vitamins, neonatal hypoprotrombine and hemorrhage¹⁵. No adequate studies have been performed on the use of Aesculus Hippocastanum (with venotonic, vascular, anti-inflammatory and antioxidant properties), Ruscus Aculeatus (venotonic, anti-inflammatory and astringent properties) and Hamamelis Virginiana (with astringent, anti-inflammatory properties, hemostatic)²¹.

Anti-inflammatory drugs are often used by patients to obtain a rapid regression of the symptoms, but the assumption of these medication is related to the possibility of complications. The prolonged use of topical steroid preparations is associated with the onset of allergic reaction and sensitization. The most commonly used

anti-inflammatory drugs are corticosteroids and non-steroidal anti-inflammatory drugs (NSAIDs), which can only be used after breastfeeding or in the absence of breast-feeding. There are not enough scientific evidences that support the safety and the effective control of the symptoms due to steroidal anti-inflammatory drugs, whether if taken orally, topically with creams or with suppositories²². Several studies demonstrated that the teratogenic effect of oral corticosteroids is dose-dependent and four case-control retrospective studies have shown association of corticosteroids assumption with the development of cleft palate²³. Anne-Mette Bay Bjørn²⁴ emphasized that the use of inhaled corticosteroids during pregnancy was associated with a slight increase in the risk of spontaneous abortion, while oral corticosteroids were not related to an increase of congenital malformations. Abramowitz recommends corticosteroids at the dose of 40mg / day for 3-5 days in pregnant women with thrombotic hemorrhoids and important edema before and after delivery, because breastfeeding contraindicates NSAID use. Although betamethasone is the most commonly used corticosteroid in clinical practice, dexamethasone showed similar efficacy²⁵. In a study of 1124 newborns was observed an increase in the likelihood of neurological alterations associated with prenatal exposure to dexamethasone, compared to betamethasone and placebo²⁶. Paracetamol (acetaminophen) can be prescribed without limitation, and at the usual dose, to reduce painful symptoms. Codeine can only be used in the 1st and 2nd trimesters of pregnancy, for a limited time, and is contraindicated during lactation. Tramadol treatment is only allowed in the 2nd trimester²⁷. The application after each defecation of topical anesthetics such as benzocaine, dibucain and pramoxine can improve anal itching and discomfort with possible onset of sensitization following prolonged use¹⁵. Inflamed hemorrhoids respond very well to sitz-baths, that reduce the tone of the internal sphincter, improve venous congestion, edema and inflammation with good symptomatic control. In 1993 Shafik et al²⁸ underlined the association between sitz-baths and the reduction of pain due to the relaxation of the internal anal sphincter, based on the theory of "thermosphere reflex". At this day there are insufficient data in the literature about the use of hot or cold water in the execution of sitz-baths. In 2010, a study on two groups of patients with acute anal pain due to hemorrhagic disease or anal fissure (24 patients in total, 12 for each group) who had used cold water (group 1, 10.8 °C (range 5-13) and hot water (group 2, 38.5 °C (range 20-40), did not highlight any differences in the clinical course of the disease, despite an improvement in painful symptoms with the use of hot water was noticed²⁹. El Ashaal et al³⁰ showed, in a study conducted in 1997, that the topical application of ice reduces pain, thanks to its anesthetic effect. This study included treatment of patients with hemorrhagic disease using the "frozen finger" of a sterile glove.

All the fingers of the glove, except for the index, had been knotted at the base, and the glove was then overturned, filled with water, ligated to the wrist and frozen, and the frozen and lubricated finger was put while the bulkiest part of the glove was external. According to El Ashaal, the analgesic action of cold acted by reducing cellular metabolism and sensory nerve transmission, inducing sphincter relaxation; furthermore local vasoconstriction helped the decrease of edema and swelling of the tissue. There are no sufficient studies on the use of low molecular weight heparin and other antithrombotic drugs which are commonly used in the case of thrombotic hemorrhoids to promote thrombolysis and improve microcirculation¹. Phlebotonic drugs have been widely prescribed for the treatment of hemorrhagic disease. The family of phlebotonic drugs belongs to natural medicines extracted from plants (such as oxerutin, diosmin, exepidine, coumarin, ruthenium, quercetin) and synthetic drugs (weakened calcium). Phlebotonics act as antioxidants, exert a protective action against inflammatory mediators, improve venous tone and lymph drainage. Alonso-Coello et al³¹ evaluated the impact of flavonoids on symptomatic hemorrhoids disease, the use of these drugs was associated with good control of symptoms such as bleeding, itching and recurrence. Since 1970, flavonoids have been used in the treatment of hemorrhoids disease in pregnancy. According to a study conducted by Jiang and Cao, MPFF (purified and micronized flavonoic fraction) was proven to be effective in reducing pain and bleeding in patients with hemorrhoids, as well as good tolerability. There were no risks in complications of fetal development, birth weight and postnatal feeding associated with the use of Dafflon 500mg¹⁵. Abramowitz³² recommends the use of micronized diamines (Dafflon) at a dose of 2-3 g / day for short periods and not for prolonged use. Several studies on the use of Rutoside, a flavonoic glycoside, in pregnancy-related hemorrhoid (I-II grade) pathology, showed significant improvement in pain relieving, compared to placebo. No significant difference in adverse reactions, fetal death, premature delivery, congenital malformations were shown compared to placebo. The most common adverse reactions reported were nausea, dizziness, gastrointestinal discomfort, vomiting, dry mouth, constipation, headache and fatigue. Lacroix et al³³ published first epidemiological data about possible effects of veinotonics in pregnancy woman. They found no increased risk of adverse pregnancy outcome among women exposed to veinotonics compared with unexposed pregnant women. Vazquez³⁴ contraindicated the use of Rutoside during the first trimester, with further studies needed. One year later, a study by Kubicsek³⁵ showed the association between Rutoside and congenital hydrocephalus. According to a double-blind, randomized controlled trial, weakened calcium, a phlebotonic drug with anti-haemodynamic action, is effective in controlling acute phase of hemorrhoids, with significant improve-

ment in inflammation³⁶. Dobesilated calcium (calcium 2,5-dihydroxybenzenesulfonate) has been extensively used in the treatment of chronic venous insufficiency and diabetic retinopathy. This drug acts by inhibiting the synthesis of PGF1a, PGF2a, PGE2, and TXB2, with dose-dependent activity³⁷. However, the use of weakened calcium can lead to important adverse reactions: several cases of agranulocytosis are well documented in literature³⁸. No sufficient studies have been conducted regarding the safety profile and the teratogenicity of the weakened calcium in pregnancy.

A pilot study by Tamas et al³⁹ revealed that calcium Dobesilate influences the blood pressure and consequently decreases the requirement for medication and hospitalization in case of mild to moderate midtrimester hypertension. Heparan sulfate (HS) is a linear polysaccharide composed of 50-200 glucosamine and uronic acid (glucuronic acid or iduronic acid) disaccharide repeats with epimerization and various sulfation modifications. HS is covalently attached to core proteins to form HS-proteoglycans. Many studies have revealed that HS critically regulates angiogenesis by playing a proangiogenic role, and this regulatory function critically depends on HS fine structure patients suffering from chronic venous disease were treated for 30 days with heparan sulphate 100 mg per os, showed an increased fibrinolytic activity and a reduced antithrombin III consumption, both of which were statistically significant⁴⁰. According to a study conducted by Italian De Cecco⁴¹, the use of eparan sulfate tablets has been shown to be more effective than oxerutin in reducing hyperemia and mucus secretion in patients with hemorrhoids.

Mesoglycan is a substance obtained from cow lung or cow blood vessel (aorta) or pig intestine. It is used as medicine for various blood vessel disorders The exact mechanism of mesoglycan, a glycosaminoglycan mixture is unknown. However, it has a profibrinolytic action and microrheologic and macrorheologic benefits.

Mesoglycans also have properties that inhibit neutrophil adhesion and activation, and enhancement in the process of wound healing⁴². Gallo et al⁴³ have evaluated the efficacy of mesoglycan in the post-operative period of patients who underwent open excisional diathermy haemorrhoidectomy. The antithrombotic properties of mesoglycan have led to a reduction in post-operative pain and an early resumption of autonomy, probably due to the reduction in thrombosis of the mucocutaneous bridge. They concluded that the use of mesoglycan, a polysaccharide complex with antithrombotic and profibrinolytic properties, can reduce the rate of post-operative thrombosis and consequently post-operative pain 7-10 days after the procedures, improving patient quality of life and speeding up the recovery of daily activities. Abramowitz et al³² recommended that it is advisable to correct the often associated transit disorders during pregnancy; they concluded that veinotonics (diosmine) can be prescribed as a short course.

TABLE I - Therapeutic options during pregnancy and post partum.

Transit Regulators:

- constipation (most often): osmotic natural (Psyllium-based) laxatives (polyethylene glycol (PEG) and lactulose), fibers (2-3 spoons of wheat bran per meal)
- if diarrhea: transit inhibitors

Physical activity

Anti-inflammatory drugs:

- corticosteroids in pregnancy and lactation (Betamethasone 40mg / day for 3-5 days)
- Corticosteroids or NSAIDs if post-partum without breastfeeding

Basic analgesics are paracetamol if resistant pain

Flebotonics (Micronized Diosmine (Daflon) at a dose of 2-3 g / day for short periods, Rutoside (Venoruton) not recommended in the first trimester

Sitz-baths, frozen finger ("frozen finger"), anesthetic gel (xylocaine)

If painful thrombosis: Diclofenac and Ibuprofen can be used up to 30th week

Refractory cases: excision or incision and evacuation of the thrombus

The treatment of hemorrhoids during pregnancy should be of conservative, with the improvement of dietary habits and with the use of suppositories or ointments. The procedure of sclerotherapy (injection of sclerosing substances at the level of the hemorrhagic plexus) during pregnancy is debated. After delivering, with the regression of predisposing factors, hemorrhoids regress spontaneously within two months in most cases^{44,45}. Invasive techniques during pregnancy are validated in case of significant bleeding and strong pain unresponsive to usable analgesics. Hemorrhoids thrombosis is thrombosis of the caudal hemorrhoid cushion that protrudes along the anal edge and the anal canal. The causes of a thrombosis can be all the conditions that lead to an increase of intra-abdominal pressure (excessive efforts during defecation, final stage of pregnancy, vaginal delivery, etc.) combined to unhealthy eating habits and diarrhea. Frequently none of the above causes are recognizable. Hemorrhoid thrombosis occurs with sudden pain associated with swelling at the level of the anal margin: diagnosis is easily confirmed by the examination of the perianal region. In the case of patients with poor symptoms, surgery is usually unnecessary. The purpose of therapy is to reduce pain through a systemic anti-inflammatory treatment with non-steroidal anti-inflammatory drugs. Diclofenac and Ibuprofen can be used until the 30th week of pregnancy. Paracetamol (up to 3x1000 mg/d) can be used for the entire duration of pregnancy. In addition to the systemic treatment, anesthetic ointments (Procain, Bupivacain, Lidovain, Mepivacain) and local cooling can

be used. With this conservative therapy, the pain should disappear in a few days, with the persistence of the nodule that should regress spontaneously in 2/4 weeks⁴⁶. In rare cases, necrosis of the vascular wall and skin is associated with spontaneous resolution of the thrombus with resolution of the symptoms. In acute situations due to the severe pain and the presence of a large thrombus, local anesthesia is used for surgical treatment, which involves the complete excision of the whole thrombosed hemorrhoid. Incision and drainage of the thrombus is not recommended due to the possibility of recurrence^{47,48}. Some authors advise to excise a part of the wall of the ectatic vessel to avoid recurrence.

Conclusion

Hemorrhoids are the most frequent anorectal pathology during pregnancy, especially in the third trimester⁴⁹. Treatment of hemorrhoids during pregnancy (Table I) is initially based on a conservative approach. As with the general population, the main risk factor is refractory constipation, which is accompanied by possible traumatic vaginal delivery. It is therefore essential to recommend regularization of intestinal transit through hygienic-dietary rules (increase dietary fiber intake, drink at least 1.5 l of water per day) and the administration of laxatives to patients with refractory constipation during pregnancy especially in post-partum, in order to reduce the risk of symptomatic hemorrhoids. Local interventions such as sitz-baths, ice, or ointments containing anesthetics, phlebotonics or glucocorticoids alone or in combination may lead to short-term relief in symptomatic patients but, as well as regularization of the transit, have no effect on prolapse and other structural alterations underlying hemorrhoid disease. Treatment with rutenium, a family of flavonoids, seems to be effective in relieving symptoms in pregnant women with hemorrhoids of the 1st and 2nd grade, but it is still not possible to assess the safety of this drug in pregnancy. Surgery for intractable disease should be postponed until the fetus is vital or even better until after childbirth. External hemorrhoids with acute strangulation thrombosis require urgent excision. Both excision and incision of hemorrhoids should be performed in local anesthesia in left side position.

Riassunto

OBIETTIVO: Le emorroidi sono delle vene varicose del retto ricoperte da mucosa in corrispondenza o in prossimità del canale anale. Normalmente sono asintomatiche, possono manifestarsi a qualsiasi età e interessano sia i maschi che le femmine. Le emorroidi sono comuni nelle giovani donne e durante la gravidanza e il puerperio. In questa recensione, affrontiamo il problema dell'approc-

cio dell'ostetrico e del chirurgo alle emorroidi e alla loro gestione nelle donne in gravidanza.

METODI: La ricerca bibliografica comprendeva tutti gli articoli pubblicati inerenti; sono stati inclusi anche abstract. Non è stata effettuata alcuna selezione della lingua. I termini di ricerca utilizzati sono stati: "emorroidi", "terapia emorroidaria", "emorroidi in gravidanza", "complicazione emorroidaria". La ricerca sui dati è stata condotta utilizzando MEDLINE, EMBASE, Web of Sciences, Scopus, Clinical Trial. gov, OVID e Cochrane Library interrogano tutti gli articoli relativi al trattamento delle emorroidi in gravidanza.

RISULTATI: Integratori di fibre, ammorbidenti delle feci e i lassativi delicati sono generalmente sicuri per le donne in gravidanza. I farmaci topici o i flebotonici orali possono essere usati con particolare cautela perché mancano prove evidenti della loro sicurezza ed efficacia in gravidanza. In caso di emorragia massiccia, il packing anale potrebbe essere una manovra semplice e utile. L'emorroidectomia è riservata alle emorroidi strangolate o ampiamente trombizzate e alle emorroidi con sanguinamento intrattabile.

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