



Journal of Coloproctology

www.jcol.org.br



Review Article

Evidence-based review of methods used to reduce pain after excisional hemorrhoidectomy



Sameh Hany Emile

Mansoura Faculty of Medicine, General Surgery Department, Mansoura City, Egypt

ARTICLE INFO

Article history:

Received 20 June 2018

Accepted 3 October 2018

Available online 6 November 2018

Keywords:

Excisional hemorrhoidectomy

Pain

Relief

Avoid

Methods

Review

ABSTRACT

Background: Excisional hemorrhoidectomy is one of the most commonly performed anorectal procedures. Despite the satisfactory outcomes of excisional hemorrhoidectomy, the pain perceived by the patients following the procedure can be a distressing sequel. This review aimed to search the current literature for the existing evidence on how to avoid or minimize the severity of post-hemorrhoidectomy pain.

Methods: An organized literature search was performed using electronic databases including PubMed/Medline and Google Scholar service for the articles that evaluated different methods for pain relief after excisional hemorrhoidectomy. Then, the studies were summarized in a narrative way illustrating the hypothesis and the outcomes of each study. The methods devised to reduce pain after excisional hemorrhoidectomy were classified into three main categories: technical tips; systemic and topical agents; and surgical methods. The efficacy of each method was highlighted along the level of evidence supporting it.

Results: Stronger evidence (level Ia) supported LigaSure hemorrhoidectomy and the use of glyceryl trinitrate ointment to be associated with significant pain relief after excisional hemorrhoidectomy whereas the remaining methods were supported by lower level of evidence (level Ib).

Conclusion: The use of LigaSure in performing excisional hemorrhoidectomy and the application of topical glyceryl trinitrate ointment contributed to remarkable relief of postoperative pain after excisional hemorrhoidectomy according to the highest level of evidence. Perhaps a multimodality strategy that combines systemic and topical agents can be the optimal method for control of pain after excisional hemorrhoidectomy, yet further prospective trials are required to draw such conclusion.

© 2018 Sociedade Brasileira de Coloproctologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

E-mail: sameh200@hotmail.com

<https://doi.org/10.1016/j.jcol.2018.10.007>

2237-9363/© 2018 Sociedade Brasileira de Coloproctologia. Published by Elsevier Editora Ltda. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Revisão baseada em evidências de métodos utilizados para reduzir a dor após hemorroidectomia excisional

R E S U M O

Palavras-chave:

Hemorroidectomia excisional
Dor
Alívio
Evitar
Métodos
Revisão

Introdução: A hemorroidectomia excisional (HE) é um dos procedimentos anorretais mais comumente realizados. Apesar dos resultados satisfatórios da hemorroidectomia excisional, a dor percebida pelos pacientes após o procedimento pode ser uma seqüela angustiante. Esta revisão teve como objetivo buscar na literatura atual as evidências existentes sobre como evitar ou minimizar a gravidade da dor pós-hemorroidectomia.

Métodos: Uma busca organizada da literatura foi realizada usando bancos de dados eletrônicos, incluindo PubMed/Medline e Google Scholar, para os artigos que avaliaram diferentes métodos para o alívio da dor após hemorroidectomia excisional. Em seguida, os estudos foram resumidos de forma narrativa, ilustrando a hipótese e os resultados de cada estudo. Os métodos desenvolvidos para reduzir a dor após a hemorroidectomia excisional foram classificados em três categorias principais: dicas técnicas; agentes sistêmicos e tópicos; e métodos cirúrgicos. A eficácia de cada método foi destacada ao longo do nível de evidência que a suporta.

Resultados: Evidências mais fortes (nível Ia) apoiaram a hemorroidectomia de LigaSure e o uso de pomada de trinitrato de glicerila para ser associado com alívio significativo da dor após hemorroidectomia excisional, enquanto os métodos restantes foram apoiados por menor nível de evidência (nível Ib).

Conclusão: O uso de LigaSure na realização de hemorroidectomia excisional e a aplicação de pomada tópica de gliceril trinitrato contribuíram para o notável alívio da dor pós-operatória após hemorroidectomia excisional, de acordo com o maior nível de evidência. Talvez uma estratégia multimodal que combine agentes sistêmicos e tópicos possa ser o método ideal para o controle da dor após hemorroidectomia excisional, mas ainda são necessários mais estudos prospectivos para chegar a essa conclusão.

© 2018 Sociedade Brasileira de Coloproctologia. Publicado por Elsevier Editora Ltda. Este é um artigo Open Access sob uma licença CC BY-NC-ND (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

Background

Excisional hemorrhoidectomy (EH) is a commonly performed procedure worldwide. Although it has been considered the most efficient method for the treatment of hemorrhoids attaining low recurrence rates¹; postoperative pain can be dreadful for some patients. In this review we attempt to shed light on the methods that can prevent or reduce the severity of post-hemorrhoidectomy pain.

Search strategy

A literature search was conducted using the PubMed/Medline and Google Scholar databases querying the following keyword: “hemorrhoid”, “excisional”, “Hemorrhoidectomy”, “Pain”, “Milligan-Morgan”, “relieve”, “medications”, “sphincterotomy”, “lateral internal sphincterotomy”, “anal dilatation”. The relevant articles and their list of references were screened for the methods used to prevent or to alleviate post-hemorrhoidectomy pain. Articles assessing other techniques of hemorrhoidectomy other than EH (e.g., stapled hemorrhoidectomy, Doppler-guided hemorrhoidal artery ligation) were excluded.

Causes of post-hemorrhoidectomy pain

The exact cause of pain arising after EH is not yet determined and appears to be multifactorial. A number of theories were proposed to explain post-hemorrhoidectomy pain. At the top of the list comes the spasm of the Internal Anal Sphincter (IAS) after exposure of its fibers, other contributing factors include the insertion of anal pack, injury of the nerve endings or the mucosal lining of the anal canal, suturing at the pedicle or below the dentate line, wound infection, and development of anal fissure.^{2,3} A rare recorded cause of persistent pain after open hemorrhoidectomy is the formation of traumatic neuroma that can cause painful symptoms that last for several year after the procedure.⁴

It was presumed that EH results in exposure of the fibers of the external and the internal anal sphincters leading to a spasm of both sphincters. While the postoperative spasm of the external sphincter is usually weak and temporary; the IAS spasm can last for a longer time. IAS spasm can be due to the exposure of its fibers after surgery with continuous irritation by fecal matters, or due to involvement of some of its fibers in the suture bite.⁵ The persistence of IAS spasm after healing of the excised area can eventually lead to an anal fissure which can be the cause of persistent long-term pain after EH.

The dentate line divides the anal canal into two equal halves, the upper half is lined by mucosa that is supplied by autonomic nerves, rendering it insensitive to pain, whereas the lower half is lined by modified skin that is supplied by somatic nerves, thus is sensitive to pain.⁶ This anatomic background is important to understand how a mistaken suture below the dentate line can result in severe postoperative pain.

As an old dictum, surgeons used to fill the anal canal with gauze or sponge as a hemostatic pack after EH. While this maneuver would somehow help prevent post-hemorrhoidectomy bleeding; the irritation and pressure induced by the pack on the sensitive mucosa and nerve endings of the anal canal would increase the patient's discomfort and factor in increased postoperative pain.

Pattern of post-hemorrhoidectomy pain

Two patterns of pain have been recognized after EH: rest pain and defecation pain. Rest pain affects the majority of the patients and occurs spontaneously without attempt of straining or defecation. It is usually most severe in the first 24 h after EH then its intensity tends to decline gradually starting from the second postoperative day onwards. Defecation pain occurs during or after defecation as a result of irritation of the anal wound by fecal matter combined with the spasm of the IAS. Patients usually experience defecation pain on the second or third postoperative day, representing a second peak of anal pain after the first peak (rest pain) has diminished.⁵

Methods of preventing or reducing pain after EH

We can broadly classify the methods by which post-hemorrhoidectomy pain can be prevented or alleviated into three main categories: technical tips; systemic and topical agents; and surgical methods.

Technical tips

Considering the technique of EH, it was suggested that closed (Ferguson) hemorrhoidectomy may cause more postoperative pain than open (Milligan-Morgan) technique^{7,8}; however, other investigators⁹ concluded that closed hemorrhoidectomy conferred less pain and faster healing in the early postoperative period. On the other hand, Arbman et al.¹⁰ disclosed that the closed technique has no advantage in postoperative pain relief as compared with the open technique.

The instruments utilized in performing the procedure may play a pivotal role in the development of postoperative pain and its degree. Andrew and colleagues¹¹ reported that using electrocautery (diathermy) has no significant advantage over the scissor dissection method in performing open hemorrhoidectomy. A randomized controlled trial¹² demonstrated comparable outcomes in terms of postoperative pain after diathermy and Harmonic scalpel hemorrhoidectomy.

On the other hand, pain after LigaSure hemorrhoidectomy has been found to be significantly less than other counterparts owing to the minimal thermal damage imposed by

LigaSure to the surrounding tissues. Altomare and coworkers¹³ described LigaSure Milligan-Morgan hemorrhoidectomy as an effective method for the treatment of grade III/VI hemorrhoids attaining less postoperative pain and faster return to work than diathermy hemorrhoidectomy. The same was reported by Muzi and colleagues¹⁴ who reported that LigaSure hemorrhoidectomy provided lower complication rate, faster wound healing, and reduced postoperative pain. Furthermore, a meta-analysis¹⁵ concluded that LigaSure hemorrhoidectomy is characterized by limited postoperative pain, shorter hospitalization and faster wound healing than the diathermy hemorrhoidectomy. Moreover, LigaSure hemorrhoidectomy achieved less postoperative pain and shorter operation time compared to Harmonic scalpel hemorrhoidectomy according to Kwok and associates.¹⁶

Certain technical points should be considered while performing EH whatever the instrument used. The primary skin incision should be as narrow and limited as possible and preferably should begin from the inside of the anal canal.⁵ Overzealous excision of the anoderm will not only result in higher degree of postoperative pain, but also may cause anal stenosis on the long run. The excision of the mucosal lining of the anal canal should be minimized as mucosal injury has been recognized to contribute to increased postoperative pain.³

In light of the anatomy of the anal canal⁶ surgical manipulations and sutures should be placed in the insensitive zone of the anal canal, above the dentate line. Maintaining adequate hemostasis by electrocautery or by sutures is mandatory to avoid the insertion of gauze pack that would cause substantial discomfort and pain to the patient postoperatively. Advising the patient to take hot Sitz bath after EH has been associated with significant relief of postoperative pain as Sitz bath help removes the wound discharge, relaxes the IAS, and increases blood flow, hence accelerating wound healing. However, Yang⁵ recommended Sitz bath only after a motion since hot water can worsen the anal wound by causing edema of the anus.

Systemic and topical agents

The use of several medications during or after EH for the reduction of postoperative pain has been extensively discussed in the literature.

Analgesics and anesthetic medications

Analgesics such as ketorolac can achieve adequate control of post-hemorrhoidectomy pain, whether administered locally or systemically. Injection of ketorolac directly into the IAS fibers serves to inhibit its spasm by suppressing the prostaglandin formation in addition to its anti-inflammatory effect.⁵ O'Donovan and colleagues¹⁷ reported that combined oral administration and local injection of ketorolac after EH achieved equivalent pain control to that of the narcotics group. Yeh et al.¹⁸ reported that sebacoyl Dinalbuphine Ester Extended-Release Injection achieved a statistically significant long-lasting reduction in pain intensity up to seven days after hemorrhoidectomy as compared to a placebo.

Patient-Controlled Analgesia (PCA) has the advantage of being controlled by the patients themselves. Although Hancke et al.¹⁹ demonstrated the superiority of PCA over conventional pain therapy in reducing the severity of pain within 24 h after EH; the large amounts of anesthetic medications to be administered rendered it less suitable as a pain control method after a simple day-case procedure as EH.⁵ Alternatively, Goldstein and associates²⁰ reported satisfactory pain control in 21 of 22 patients who used subcutaneous morphine pump after EH, the authors described subcutaneous morphine pump as a cost-effective method for satisfactory pain control after EH.

Local application of opioid was advocated by Tegen and colleagues²¹ who randomly divided 135 patients with hemorrhoids into three groups; the first received topical morphine application, the second received topical oxycodone and the third received vehicle embedded in a sponge lift in the anus. The study came to a conclusion that local administration of very low doses of kappa-opioid agonist decreased pain after EH effectively; this was presumed to occur through interaction with specific opioid receptors on the anal mucosa.

Local infiltration of the skin around the anal verge with long-acting anesthetic as bupivacaine can also decrease the severity of post-hemorrhoidectomy pain. Haas et al.²² have compared between the local infiltration of bupivacaine HCl and Liposome Bupivacaine (LB) after EH and concluded that LB resulted in significantly reduced postoperative pain compared with bupivacaine HCl. In line with the former trial, a multicenter randomized controlled study²³ reported that bupivacaine extended-release liposome offered significant reduction in pain scores through 72 h after EH, with decreased opioid requirements, and improved patient satisfaction compared with a placebo.

In addition to local infiltration, local anesthetic agents can be applied in the form of cream. Topical EMLATM cream, which is composed of lidocaine 2.5% and prilocaine 2.5%, was investigated by Shiau and colleagues²⁴ and was found to decrease pain after EH and to reduce the dosage of analgesic injections compared to the control group that received neomycin ointment. In addition, no systemic complications were observed after the application of EMLATM cream.

Field block using local anesthetic agents has been also reported. Rajabi and colleagues²⁵ found preemptive ischorectal block with bupivacaine significantly reduced post-hemorrhoidectomy pain. In accord, Brunat and associates²⁶ suggested that posterior perineal block with ropivacaine 0.75% is a simple, effective method for pain control after EH providing better postoperative analgesia than PCA alone. Pudendal nerve block with local bupivacaine has been devised by Imbelloni and coworkers²⁷ as an effective method to relieve pain after EH, the authors reported excellent analgesic effect with low need for opioids and without local or systemic complications or urinary retention.

Flavonoids

Micronized Purified Flavonoid Fraction (MPFF), when used in combination with antibiotic and anti-inflammatory medications, can reduce the duration and extent of post-hemorrhoidectomy pain and bleeding as demonstrated by two randomized controlled clinical trials.^{28,29} MPFF consists of

diosmine (90%) and flavonoids expressed as hesperidin (10%). The micronization allows higher absorption from the gastrointestinal tract giving it superiority over other flavonoids. MPFF decreases pain and bleeding after EH by inhibiting the inflammatory process, reducing edema, improving venous tone, and protecting the microcirculations from the inflammatory mediators.²⁸

Antibiotics

Metronidazole has been recognized to decrease pain after EH. When administered systemically, metronidazole is reported to relieve post-hemorrhoidectomy pain because of its antimicrobial action that reduces the bacterial colonization at the surgical sites, in addition to its anti-inflammatory effects as well. The pain-relieving effect of systemic metronidazole is debatable as Solorio-López et al.³⁰ proved that oral administration of metronidazole 500 mg can effectively reduce pain after EH compared with a placebo. In contrast, Khan and colleagues³¹ concluded that prophylactic antibiotics, including metronidazole, have no tangible role in pain relief after open hemorrhoidectomy. Additionally, Balfour et al.³² disclosed that the systemic application of metronidazole 400 mg three times per day after closed hemorrhoidectomy did not reduce the postoperative pain.

Topical metronidazole ointment has the privilege of higher tissue concentration along with less systemic side effect than the oral medication. In placebo-controlled randomized study, Ala and affiliates³³ found that topical application of metronidazole 10% significantly reduced discomfort after EH up to 14 days, and alleviated postoperative pain during defecation as compared to the placebo group. Nicholson and Armstrong³⁴ also reported significant reduction of post-hemorrhoidectomy discomfort and edema after using topical metronidazole 10%. Another topical antimicrobial that was devised for the reduction of post-hemorrhoidectomy pain is triclosan which was investigated in a multi-center double blind randomized trial³⁵ and was found to improve the control of post-operative symptoms, including pain, and wound healing compared to sodium hypochlorite.

Sucralfate and cholestyramine

In addition to topical antimicrobials, other topical agents have been advocated for the relief of post-hemorrhoidectomy pain. Sucralfate reduces pain after EH by promoting wound healing owing to its angiogenic effects and to its inhibitory effect on the degradation of fibroblast.⁵ Gupta et al.³⁶ concluded that topical sucralfate significantly reduced pain after EH up to two weeks postoperatively and provided faster wound healing compared with that of a placebo. The findings of Gupta and colleagues were reproduced by another double-blind randomized study³⁷ which disclosed that sucralfate ointment significantly reduced the acute postoperative pain after EH more than the placebo group.

Similarly, topical application of cholestyramine ointment 15% conferred less postoperative pain at 24 and 48 h after EH, lower pain during defecation, and less analgesic requirement than the placebo group.³⁸ Cholestyramine is used for treating perianal skin irritation because of its bile acid-binding

activity since the bile acids secreted in the stool are the major cause of perianal skin irritation.³⁹ Wang and Hua⁴⁰ suggested that Chinese herbal fumigation and washing could reduce the postoperative pain and edema, and could shorten the time of wound healing after EH compared to the control group.

Chemical sphincterotomy

Since the IAS spasm was thought to be the major factor contributing to pain after EH^{2,3}; topical medications that induce direct relaxation of the IAS or what is called chemical sphincterotomy were tried to decrease the degree of pain after EH. A literature review by Siddiqui and colleagues⁴¹ identified three different categories of these medications: calcium channel blockers, Glyceryl Trinitrate (GTN), and botulinum toxin. The review concluded that the three categories were effective in pain control up to one week after hemorrhoidectomy compared to a placebo.

Few trials evaluated calcium channel blockers in pain reduction after EH. Three placebo-controlled randomized trials^{42–44} used topical diltiazem 2%, whereas one randomized study⁴⁵ used nifedipine 0.3%. While both diltiazem and nifedipine provided significantly less pain at 7 days after EH, Perrotti et al.⁴⁵ reported higher rate of complications, including fecal incontinence that was 2.4% after the use of Nifedipine 0.3% combined with lidocaine 1.5%.

Ratnasingham and associates⁴⁶ conducted a meta-analysis of the analgesic effect of GTN ointment after EH and concluded that GTN did not only manage to decrease post-hemorrhoidectomy pain significantly at three and seven days postoperatively, but it also had an Odds Ratio of 3.57 for wound healing compared with the placebo. The only drawback of using GTN was a higher incidence of headache after its application (OR = 3.41).

Injection of botulinum toxin in the IAS has been described in a few randomized trials.^{47–49} It is worthy to notice that up to 5 days after EH there were conflicting results among these trials. While Davies et al.⁴⁷ and Singh et al.⁴ found no significant difference in the pain scores up to day 5, Patti and coworkers⁴⁹ observed a significantly lower pain score in the botulinum toxin group within the first five days after surgery. Beyond day 6, all of the trials concurred on reporting that the botulinum toxin group had remarkably lower overall pain score than the placebo group.

Another topical agent that help relaxes the IAS after EH is trimebutine. In a randomized study, Ho and colleagues⁵⁰ compared the application of trimebutine suppository after EH with a control group that did not receive a suppository and observed that although trimebutine managed to reduce the mean resting anal pressure significantly at four hours after application; no differences in the pain scores at 4, 24, and 48 h between the two groups were noted.

Gabapentin

Gabapentin was originally prescribed as an anticonvulsant medication, yet it proved to be effective in alleviating neuropathic pain, such as diabetic neuropathy. It was thought that gabapentin exerts its analgesic effect through central neuronal sensitization however; the mechanism of action of

gabapentin in pain relief is still not completely understood. Poylin and colleagues⁵¹ investigated the analgesic effect of gabapentin on 21 patients with hemorrhoids who underwent EH whereas 18 patients were assigned in the control group. According to the authors, the treatment group of gabapentin had significantly lower pain scores at 1, 7, and 14 days postoperatively. Moreover, no gabapentin-related complications or adverse effects were recorded. The authors described gabapentin as an inexpensive, effective method to improve pain after hemorrhoidectomy, yet they recommended further prospective randomized trials to better define the clinical usefulness of this medication.

Electric nerve stimulation

Transcutaneous Electrical Nerve Stimulation (TENS) was found to effectively relieve pain in patients undergoing EH. Chiu et al.⁵² conducted a randomized study comparing 30 patients who received TENS after EH with an equal number of patients who did not receive TENS. The TENS group had significantly lower subjective pain scores up to 24 h, and required less amount of morphine than the control group. The pain-relieving effect of TENS was attributed to the increased release of endogenous morphines as 13 endorphin, enkephalin, and dynorphin as a result of the peripheral electro-acupunctural stimulation.⁵³

Miscellaneous topical agents

Topical application of Vitamin E has been devised by Ruiz-Tovar and colleagues⁵⁴ who concluded that the application of vitamin E ointment after Milligan-Morgan hemorrhoidectomy managed to reduce postoperative pain, and hospital stay. The authors explained the pain-alleviating effect of vitamin E that it reduced the associated edema and moderated the increase of cyclooxygenase-2 enzyme thus, decreased the synthesis of prostaglandin E2, an important mediator for the local inflammatory response.

Froehner Junior and associates⁵⁵ evaluated the pain-relieving effects of topical policresulen and cinchocaine after open hemorrhoidectomy. Compared to the control group, the authors found no significant reduction of pain scores after the topical application of policresulen and cinchocaine at all time points of the study up to 15 days postoperatively. Policresulen contributes to the process of wound healing through its antimicrobial action and chemical debriding effects, on the other hand cinchocaine (dibucaine) is a topical anesthetic of the amide group that acts rapidly, within 15 min, achieving a local anesthetic effect that lasts for 2 to 4 h.⁵⁶

Sim and Tan⁵⁷ conducted a randomized single-blind clinical trial on the efficacy of the intradermal injection of methylene blue after diathermy hemorrhoidectomy. Thirty-seven patients were in the methylene blue group and 30 were in the placebo group. The treatment group had significantly less pain scores and required less amount of paracetamol than the placebo group in the first three days postoperatively. However, after the third postoperative day there were no notable differences in the mean pain scores between both groups. The authors suggested that perianal intradermal injection of methylene blue would ablate the perianal dermal

Table 1 – Summary of the agents used for pain relief after excisional hemorrhoidectomy.

Agent	Mechanism of pain relief	^a Efficacy according to level of evidence
<i>Systemic agents</i>		
Analgesics (Ketorolac)	Systemic Anti-inflammatory effect through inhibition of COX-2 enzyme	Effective – Level Ib
Subcutaneous morphine pump	Continuous flow of narcotic per demand of the patients	Effective – Level Ib
Micronized purified flavonoid fraction	Inhibits the inflammatory process, reduces edema, improves venous tone, and protects the microcirculations from the inflammatory mediators	Effective – Level Ib
Antibiotics (metronidazole)	Systemic antimicrobial action preventing bacterial colonization and secondary wound infection	Controversial – Level Ib
Gabapentin	Central neuronal sensitization	Effective – Level Ib
TENS	Induce release of central neurotransmitters as 13-endorphin, enkephalin, and dynorphin	Effective – Level Ib
<i>Topical agents</i>		
Opioids (Morphine/oxycodone)	Interaction with specific opioid receptors on the anal mucosa	Effective – Level Ib
<i>Local anesthetics</i>		
ELMA cream		
Bupivacaine HCl	Long-acting local anesthetic action by reversible binding to and inactivating sodium channels thus blocking conduction in peripheral nerves.	Effective – Level Ib
Liposome bupivacaine infiltration		
Pudendal nerve block		
Antimicrobial	Local antimicrobial action preventing bacterial colonization and secondary wound infection	Effective – Level Ib
Metronidazole		
Triclosan	Antibacterial and antifungal actions	Effective – Level Ib
Sucalfate	Promotes wound healing by angiogenic effects and inhibition of the fibroblast degradation	Effective – Level Ib
Cholestyramine	Bile acid-binding activity: decreases the amount of bile acids secreted in the stool that cause perianal skin irritation	Effective – Level Ib
Chinese herbal lotion	–	Effective – Level Ib
Calcium channel blockers	Relaxation of IAS	Effective – Level Ib
GTN	(chemical sphincterotomy)	Effective – Level Ia
Botulinum toxin		Controversial – level Ib
Trimebutine		Not effective- Level Ib
Vitamin E	Reduces edema and moderates the increase of COX-2 enzyme thus, decrease the synthesis of prostaglandin E2	Effective – Level Ib
Policresulen	Antimicrobial and chemical debridement	Not effective – Level Ib
Cinchocaine	Local long-lasting anesthetic action	
Perianal intradermal injection of methylene blue	Temporal ablation of dermal nerve endings	Effective – Level Ib
Atorvastatin	Anti-inflammatory, immunomodulatory, antioxidant, and antibacterial	Effective – Level Ib
Warm plastic bags	Local heating effect help relaxes the IAS and increase the blood flow hence, accelerating healing of the perianal wound	Effective – Level Ib

COX, Cyclo-Oxygenase enzyme; IAS, Internal Anal Sphincter; GTN, Glyceryl Trinitrate.

^a Level of evidences according to Oxford center for evidence based medicine: Ia, systematic review and/or meta-analysis of randomized controlled trials; Ib, individual randomized controlled trials; IIb, individual cohort studies.

nerve endings temporarily, hence provided temporal relief of pain after EH.

Ala and associates⁵⁸ investigated the effect of topical atorvastatin on post-hemorrhoidectomy pain and wound healing. Sixty-six patients with Grade III/IV hemorrhoids undergoing open hemorrhoidectomy were randomly divided into two

equal groups: treatment group and placebo group. Although no significant differences in the mean postoperative pain scores were observed between the two groups in the first 48 h postoperatively, pain scores during defecation were significantly lower in the treatment group than in placebo. Both groups exhibited comparable pethidine and acetaminophen

requirements. Wound healing was significantly better in the treatment group at two weeks postoperatively.

Similar to the concept of hot Sitz bath, local thermal application can be used for the relief of post-hemorrhoidectomy pain as advocated by Balta and colleagues⁵⁹ in their randomized controlled study. The authors divided patients with high grade hemorrhoids undergoing LigaSure hemorrhoidectomy into two groups; the first group received warm plastic bag application after surgery whereas the control group did not receive such therapy. The postoperative pain scores for the treatment group were significantly lower than the control group at the first and the third days postoperatively.

A systematic review⁶⁰ of the topical agents used for pain control after EH concluded that the topical preparations accomplished encouraging results in reducing pain and improving wound after hemorrhoidectomy, the review recommended using the topical preparations that proved their efficacy including GTN, calcium channel blockers, metronidazole, local anesthetics, sucralfate and botulinum toxin. A summary of the medical agents described in the literature for pain relief after EH and their mechanisms of action are illustrated in [Table 1](#).

Surgical methods

Adopting the concept of chemical sphincterotomy, some surgical procedures can be combined with EH in order to weaken the spasm of the IAS that factor substantially in the development of postoperative pain. Lateral Internal Sphincterotomy (LIS) is perhaps the most popular procedure in this regard. Anal dilatation is another technique that has seldom been used nowadays because of its high rate of complications.

A number of randomized trials had compared between EH alone and EH combined with LIS aiming to elucidate the benefits and complications of LIS. A recent review⁶¹ concluded that LIS significantly reduced postoperative pain, analgesic requirements, and the incidence of postoperative urinary retention following EH. However, the authors recommended tailoring LIS to each patient and setting out certain criteria for patient selection since the patients who underwent LIS plus EH had a median fecal incontinence rate of 7.7% compared to 1.25% after EH alone. Incontinence was minor in degree and temporary in duration ranging from one week up to one year in one study.⁶² Interestingly most of the studies^{63–66} that applied open hemorrhoidectomy reported significant reduction in pain scores after adding LIS to hemorrhoidectomy, whereas the only study⁶⁷ that used closed hemorrhoidectomy did not find any significant advantage of adding LIS regarding postoperative pain.

While the role of LIS in pain relief after EH might still be controversial in some perspectives; the use of manual anal dilatation has been widely discouraged owing to the unacceptably high rates of fecal incontinence that reach up to 57%.⁶⁸

Summary and recommendations

Whatever the type of EH performed, or the instrument utilized, the most important method to reduce pain postoperatively is employing the sound technique of EH as in avoiding

overzealous excision of the skin and anal mucosa, keeping the sutures proximal to the dentate line and away from the IAS, and ensuring adequate hemostasis to avoid the insertion of anal pack.

Since the origin of post-hemorrhoidectomy pain is probably multifactorial, it appears that the strategy that needs be applied to prevent or to reduce this sequel should be a multimodality strategy as well. Multimodality pain management has been shown to decrease pain severity and reduce opioid requirements in different types of surgery.⁵¹

A combination of systemic and topical agents could potentially reduce the degree of pain more effectively than a single agent alone; yet this needs more investigations to conclude. Perhaps the postoperative systemic administration of analgesics and metronidazole or other agents as MPFF combined with the local application of one of many topical preparations described in the literature can be an optimal strategy for pain control after EH.

Regarding LIS, in light of the pattern and onset of pain that occurs after EH, it seems that chemical sphincterotomy due to its short-term temporary action, would be more appropriate since the pain after EH usually does not last long enough to justify performing permanent insult to the IAS as with LIS.

Conclusions

In summary, since there is no consensus or guidelines on how to prevent or at least minimize the severity of pain after EH; this review tried to explore the current literature looking for the most practical and effective methods in this context.

The use of LigaSure in performing EH and the application of topical glyceryl trinitrate ointment contributed to remarkable relief of postoperative pain after EH according to the highest level of evidence.

Further investigations evaluating the efficacy of multimodality strategy for pain control, as devised by the present review, are required to fulfill an important objective that is keeping patients with hemorrhoids free of pain and agony postoperatively.

Conflicts of interest

The author declares no conflicts of interest.

REFERENCES

1. MacRae HM, McLeod RS. Comparison of hemorrhoidal treatment modalities. A meta-analysis. *Dis Colon Rectum*. 1995;38:687–94.
2. Rahimi R, Abdollahi M. A systematic review of the topical drugs for post-hemorrhoidectomy pain. *Int J Pharmacol*. 2012;8:628–37.
3. Lohsiriwat D, Lohsiriwat V. Outpatient hemorrhoidectomy under perianal anesthetics infiltration. *J Med Assoc Thai*. 2005;88:1821–4.
4. Takawira C, Shenouda S, Mikuz G, Sergi C. Traumatic neuroma of the anus after Milligan-Morgan hemorrhoidectomy. *Ann Clin Lab Sci*. 2014;44:324–7.

5. Yang HK. Perioperative management. In: Yang HK, editor. Hemorrhoids. Berlin Heidelberg: Springer-Verlag; 2014.
6. Kapoor VH, Gest T, editors. Anal canal anatomy. Medscape; 2016. <http://emedicine.medscape.com/article/1990236-overview#a2> [accessed 08.08.16].
7. Ho YR, Jong HK, Nam PK. A clinical observation on 143 cases of hemorrhoids. *J Korean Surg Soc.* 1991;41:100-6.
8. Gençosmanoğlu R, Sad O, Koç D, Inceoğlu R, Hemorrhoidectomy: open or closed technique? A prospective, randomized clinical trial. *Dis Colon Rectum.* 2002;45:70-5.
9. You SY, Kim SH, Chung CS, Lee DK. Open vs. closed hemorrhoidectomy. *Dis Colon Rectum.* 2005;48:108-13.
10. Arbman G, Krook H, Haapaniemi S. Closed vs. open hemorrhoidectomy – is there any difference? *Dis Colon Rectum.* 2000;43:31-4.
11. Andrew BT, Layer GT, Jackson BT, Nicholls RJ. Randomized trial comparing diathermy hemorrhoidectomy with the scissor dissection Milligan-Morgan operation. *Dis Colon Rectum.* 1993;36:580.
12. Tan JJ, Seow-Choen F. Prospective, randomized trial comparing diathermy and harmonic scalpel hemorrhoidectomy. *Dis Colon Rectum.* 2001;44:677-9.
13. Altomare DF, Milito G, Andreoli R, Arcanà F, Tricomi N, Salafia C, et al. Ligasure Precise vs. conventional diathermy for Milligan-Morgan hemorrhoidectomy: a prospective, randomized, multicenter trial. *Dis Colon Rectum.* 2008;51:514-9.
14. Muzi MG, Milito G, Nigro C, Cadeddu F, Andreoli F, Amabile D, et al. Randomized clinical trial of LigaSure and conventional diathermy haemorrhoidectomy. *Br J Surg.* 2007;94:937-42.
15. Milito G, Cadeddu F, Muzi MG, Nigro C, Farinon AM. Haemorrhoidectomy with ligasure vs conventional excisional techniques: meta-analysis of randomized controlled trials. *Colorectal Dis.* 2010;12:85-93.
16. Kwok SY, Chung CC, Tsui KK, Li MK. A double-blind, randomized trial comparing ligasure and harmonic Scalpel hemorrhoidectomy. *Dis Colon Rectum.* 2005;48:344-8.
17. O'Donovan S, Ferrara A, Larach S, Williamson P. Intraoperative use of toradol facilitates outpatient hemorrhoidectomy. *Dis Colon Rectum.* 1994;37:793-9.
18. Yeh CY, Jao SW, Chen JS, Fan CW, Chen HH, Hsieh PS, et al. Sebacyl Dinalbuphine ester extended-release injection for long-acting analgesia: a multicenter, randomized, double blind, and placebo-controlled study in hemorrhoidectomy patients. *Clin J Pain.* 2017;33:429-34.
19. Hancke E, Lampinski M, Suchan K, Völke K. Pain management after hemorrhoidectomy. Patient-controlled analgesia vs conventional pain therapy. *Chirurg.* 2013;84:587-93.
20. Goldstein ET, Williamson PR, Larach SW. Subcutaneous morphine pump for postoperative hemorrhoidectomy pain management. *Dis Colon Rectum.* 1993;36:439-46.
21. Tegen G, Pulzato L, Passarella L, Guidolin D, Zusso M, Giusti P. Randomized placebo-controlled trial on local applications of opioids after hemorrhoidectomy. *Tech Coloproctol.* 2009;13:219-24.
22. Haas E, Onel E, Miller H, Ragupathi M, White PF. A double-blind, randomized, active-controlled study for post-hemorrhoidectomy pain management with liposome bupivacaine, a novel local analgesic formulation. *Am Surg.* 2012;78:574-81.
23. Gorfine SR, Onel E, Patou G, Krivokapic ZV. Bupivacaine extended-release liposome injection for prolonged postsurgical analgesia in patients undergoing hemorrhoidectomy: a multicenter, randomized, double-blind, placebo-controlled trial. *Dis Colon Rectum.* 2011;54:1552-9.
24. Shiau JM, Su HP, Chen HS, Hung KC, Lin SE, Tseng CC. Use of a topical anesthetic cream (EMLA) to reduce pain after hemorrhoidectomy. *Reg Anesthesia Pain Med.* 2008;33:30-5.
25. Rajabi M, Hosseinpour M, Jalalvand F, Afshar M, Moosavi G, Behdad S. Ischiorectal block with bupivacaine for post hemorrhoidectomy pain. *Korean J Pain.* 2012;25:89-93.
26. Brunat G, Pouzeratte Y, Mann C, Didelot JM, Rochon JC, Eledjam JJ. Posterior perineal block with ropivacaine 0.75% for pain control during and after hemorrhoidectomy. *Reg Anesth Pain Med.* 2003;28:228-32.
27. Imbelloni LE1, Vieira EM, Gouveia MA, Netinho JG, Spirandelli LD, Cordeiro JA. Pudendal block with bupivacaine for postoperative pain relief. *Dis Colon Rectum.* 2007;50:1656-61.
28. La Torre F, Nicolai AP. Clinical use of micronized purified flavonoid fraction for treatment of symptoms after hemorrhoidectomy: results of a randomized, controlled, clinical trial. *Dis Colon Rectum.* 2004;47:704-10.
29. Colak T, Akca T, Dirlik M, Kanik A, Dag A, Aydın S. Micronized flavonoids in pain control after hemorrhoidectomy: a prospective randomized controlled study. *Surg Today.* 2003;33:828-32.
30. Solorio-López S, Palomares-Chacón UR, Guerrero-Tarín JE, González-Ojeda A, Cortés-Lares JA, Rendón-Félix J, et al. Efficacy of metronidazole versus placebo in pain control after hemorrhoidectomy. Results of a controlled clinical trial. *Rev Esp Enferm Dig.* 2015;107:681-5.
31. Khan KI, Akmal M, Waqas A, Mahmood S. Role of prophylactic antibiotics in Milligan Morgan hemorrhoidectomy – a randomized control trial. *Int J Surg.* 2014;12:868-71.
32. Balfour L, Stojkovic SG, Botterill ID, Burke DA, Finan PJ, Sagar PM. A randomized, double-blind trial of the effect of metronidazole on pain after closed hemorrhoidectomy. *Dis Colon Rectum.* 2002;45:1186-90.
33. Ala S, Saeedi M, Eshghi F, Mirzabeygi P. Topical metronidazole can reduce pain after surgery and pain on defecation in postoperative hemorrhoidectomy. *Dis Colon Rectum.* 2008;51:235-8.
34. Nicholson TJ, Armstrong D. Topical metronidazole (10 percent) decreases posthemorrhoidectomy pain and improves healing. *Dis Colon Rectum.* 2004;47:711-6.
35. Giannini I, Pecorella G, Pennisi D, Santangelo G, Digennaro R, Latorre F, et al. Control of post-hemorrhoidectomy symptoms and wound healing by Triclosan: a randomized, double-blind, controlled trial. *Minerva Chir.* 2014;69:75-82.
36. Gupta PJ, Heda PS, Kalaskar S, Tamaskar VP. Topical sucralfate decreases pain after hemorrhoidectomy and improves healing: a randomized, blinded, controlled study. *Dis Colon Rectum.* 2008;51:231-4.
37. Ala S, Saeedi M, Eshghi F, Rafati M, Hejazi V, Hadianamrei R. Efficacy of 10% sucralfate ointment in the reduction of acute postoperative pain after open hemorrhoidectomy: a prospective, double-blind, randomized, placebo-controlled trial. *World J Surg.* 2013;37:233-8.
38. Ala S, Eshghi F, Enayatifard R, Fazel P, Rezaei B, Hadianamrei R. Efficacy of cholestyramine ointment in reduction of postoperative pain and pain during defecation after open hemorrhoidectomy: results of a prospective, single-center, randomized, double-blind, placebo-controlled trial. *World J Surg.* 2013;37:657-62.
39. Palmer RH, Glickman PB, Kappas A. Pyrogenic and inflammatory properties of certain bile acids in man. *J Clin Invest.* 1962;41:1573.
40. Wang YJ, Hua GH. Observation of curative effect of hemorrhoids lotion on pain, edema and bleeding after anorectal surgery. *Zhongguo Zhong Yao Za Zhi.* 2015;40:4497-500.
41. Siddiqui MR, Abraham-Igwe C, Shangumanandan A, Grassi V, Swift I, Abulafi AM. A literature review on the role of chemical

- sphincterotomy after Milligan-Morgan hemorrhoidectomy. *Int J Colorectal Dis.* 2011;26:685-92.
42. Amoli HA, Notash AY, Shahandashti FJ, Kenari AY, Ashraf H. A randomized, prospective, double-blind, placebo-controlled trial of the effect of topical diltiazem on post-hemorrhoidectomy pain. *Colorectal Dis.* 2011;13:328-32.
43. Silverman R, Bendick PJ, Wasvary HJ. A randomized, prospective, double-blind, placebo-controlled trial of the effect of a calcium channel blocker ointment on pain after hemorrhoidectomy. *Dis Colon Rectum.* 2005;48:1913-6.
44. Sugimoto T, Tsunoda A, Kano N, Kashiwagura Y, Hirose K, Sasaki T. A randomized, prospective, double-blind, placebo-controlled trial of the effect of diltiazem gel on pain after hemorrhoidectomy. *World J Surg.* 2013;37:2454-7.
45. Perrotti P, Dominici P, Grossi E, Cerutti R, Antropoli C. Topical nifedipine with lidocaine ointment versus active control for pain after hemorrhoidectomy: results of a multicentre, prospective, randomized, double-blind study. *Can J Surg.* 2010;53:17-24.
46. Ratnasingham K, Uzzaman M, Andreani SM, Light D, Patel B. Meta-analysis of the use of glyceryl trinitrate ointment after haemorrhoidectomy as an analgesic and in promoting wound healing. *Int J Surg.* 2010;8:606-11.
47. Davies J, Duffy D, Boyt N, Aghahoseini A, Alexander D, Leveson S. Botulinum toxin (botox) reduces pain after hemorrhoidectomy: results of a double-blind, randomized study. *Dis Colon Rectum.* 2003;46:1097-102.
48. Singh B, Box B, Lindsey I, George B, Mortensen N, Cunningham C. Botulinum toxin reduces anal spasm but has no effect on pain after haemorrhoidectomy. *Colorectal Dis.* 2009;11:203-7.
49. Patti R, Almasio PL, Muggeo VM, Buscemi S, Arcara M, Matranga S, et al. Improvement of wound healing after hemorrhoidectomy: a double-blind, randomized study of botulinum toxin injection. *Dis Colon Rectum.* 2005;48:2173-9.
50. Ho YH, Seow-Choen F, Low JY, Tan M, Leong AP. Randomized controlled trial of trimebutine (anal sphincter relaxant) for pain after haemorrhoidectomy. *Br J Surg.* 1997;84:377-9.
51. Poylin V, Quinn J, Messer K, Nagle D. Gabapentin significantly decreases posthemorrhoidectomy pain: a prospective study. *Int J Colorectal Dis.* 2014;29:1565-9.
52. Chiu JH, Chen WS, Chen CH, Jiang JK, Tang GJ, Lui WY, et al. Effect of transcutaneous electrical nerve stimulation for pain relief on patients undergoing hemorrhoidectomy: prospective, randomized, controlled trial. *Dis Colon Rectum.* 1999;42:180-5.
53. Lin JG, Chen XH, Han JS. Antinociception produced by 2 and 5 KHz peripheral stimulation in the rat. *Int J Neurosci.* 1992;64:15-22.
54. Ruiz-Tovar J, Duran M, Alias D, Manso B, Moreno A, Nevado C, et al. Reduction of postoperative pain and improvement of patients' comfort after Milligan-Morgan hemorrhoidectomy using topical application of vitamin E ointment. *Int J Colorectal Dis.* 2016;31:1371-2.
55. Froehner Junior I, Kotze PG, Rocha JG, Miranda EF, Sartor MC, Martins JF, et al. Postoperative topical analgesia of hemorrhoidectomy with policresulen and cinchocaine: a prospective and controlled study. *Rev Col Bras Cir.* 2014;41:92-8.
56. Lee AY. Allergic contact dermatitis from dibucaine in Proctosedyl ointment without cross-sensitivity. *Contact Dermatitis.* 1988;39:261.
57. Sim HL, Tan KY. Randomized single-blind clinical trial of intradermal methylene blue on pain reduction after open diathermy haemorrhoidectomy. *Colorectal Dis.* 2014;16:O283-7.
58. Ala S, Alvandipour M, Saeedi M, Hamidian M, Shiva A, Rahmani N, et al. Effects of topical atorvastatin (2%) on posthemorrhoidectomy pain and wound healing: a randomized double-blind placebo-controlled clinical trial. *World J Surg.* 2017;41:596-602.
59. Balta AZ, Ozdemir Y, Sucullu I, Filiz AI, Yucel E, Akin ML. The effect of early warm plastic bag application on postoperative pain after hemorrhoidectomy: a prospective randomized controlled trial. *Am Surg.* 2015;81:182-6.
60. Rahimi R, Abdollahi M. A systematic review of the topical drugs for post hemorrhoidectomy pain. *Int J Pharmacol.* 2012;8:628-37.
61. Emile SH, Youssef M, Elfeki H, Thabet W, El-Hamed TM, Farid M. Literature review of the role of lateral internal sphincterotomy (LIS) when combined with excisional hemorrhoidectomy. *Int J Colorectal Dis.* 2016;31:1261-72.
62. Mathai V, Ong BC, Ho YH. Randomized controlled trial of lateral internal sphincterotomy with haemorrhoidectomy. *Br J Surg.* 1996;83:380-2.
63. Diana G, Guercio G, Cudia B, Ricotta C. Internal sphincterotomy reduces postoperative pain after Milligan Morgan hemorrhoidectomy. *BMC Surg.* 2009;9:16.
64. Galizia G, Lieto E, Castellano P, Pelosio L, Imperatore V, Pigantelli C. Lateral internal sphincterotomy together with haemorrhoidectomy for treatment of haemorrhoids: a randomized prospective study. *Eur J Surg.* 2000;166:223-8.
65. Das DK, Choudhury UC, Lim ZS. Effectiveness of internal sphincterotomy in reducing post open hemorrhoidectomy pain: a randomized comparative clinical study. *Int J Collab Res Intern Med Public Health.* 2013;5:428.
66. Raza M, Khan A, Kamran R, Waqas K, Yusuf A. Hemorrhoidectomy with and without lateral internal sphincterotomy. *J Rawalpindi Med Coll.* 2013;17:189-91.
67. Khubchandani IT. Internal sphincterotomy with hemorrhoidectomy does not relieve pain: a prospective, randomized study. *Dis Colon Rectum.* 2012;45:1452-7.
68. Asfar SK, Juma TH, Ala-Edeen T. Hemorrhoidectomy and sphincterotomy. A prospective study comparing the effectiveness of anal stretch and sphincterotomy in reducing pain after hemorrhoidectomy. *Dis Colon Rectum.* 1988;31:181-5.