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Comparison of Various Analgesic Protocols for Control of Postoperative Pain Following Anorectal Surgery

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ABSTRACT

Background: Anorectal pathology is commonly perceived it and handled in common surgical practitioners' fistula and abscess, hemorrhoids, fissures, condyloma, and other pathological conditions. Because of the strong sensory innervations of the canal of anal, patients endure severe discomfort during anorectal surgery. It is generally most severe in the first twenty-four hours especially after excisional hemorrhoidectomy. the aim of this study is a comparison between different analgesic protocols used to relieve pain postoperative anorectal surgery.

Methods: PubMed, Embase, Medline, Science Gate, Scientific Report, Elsevier, Google Scholar, and Cochrane Evidence Based Medicine Reviews were used to conduct a review search. Review of newly released books and papers with regard to the topic, as well as manual searches (Comparison of various analgesic protocols for control of postoperative pain following anorectal surgery), was started at (May,2021). we searched the published studies from 2011 to the present date by the full text:(various analgesic protocols post anorectal surgery).

Results: Anorectal surgery is marked by excruciating discomfort after the procedure. Using the new technique during anorectal surgery as hemorrhoidectomy to avoid more excision of anal mucosa and the skin, putting the suture nearest to the dentate line and away from the internal anal sphincter, and good hemostasis to avoid the inserting of the anal pack are the most essential methods to lessen pain postoperatively regardless of the type of anorectal surgery performed or the instrument to use during it. We found more protocols using multimodality pain management for the relief of pain, topical drugs that produce direct relaxation of the internal anal sphincter, topical intervention as a pudendal nerve block, a method of surgery as surgical sphincterotomy, and technical tips to reduce pain as ligasure.

Conclusion: Multimodal pain treatment has been demonstrated to minimize pain intensity and opioid doses in various kinds of surgery.

According to the highest degree of proof, using current technological procedures and tools as a ligasure with some topical agent as GTN glyceryl trinitrate ointment provided amazing excellent alleviation of postoperative pain following anorectal surgery.

n the United States, about a million surgical procedures are done each year, with nearly half of them being inpatient procedures. During the first few days following surgery, most patients report moderate, severe, or excruciating pain, with 15% to 45 percent experiencing persistent postsurgical pain Effective

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postsurgical pain management is crucial for patient recovery and may lead to earlier patient mobility, shorter hospital stays, and lower health-care expenditures. To optimize relief of pain, decrease the risk of an adversative event (AEs), and enhance patient outcomes, multimodal approaches for perioperative pain management are advocated [1]. Anorectal disease is often recognized and treated by general surgery, however, data on opioids prescription after anorectal surgery is scarce. Hemorrhoids, fissures, fistula and abscess, condyloma, and other disease processes are examples of anorectal pathology. Nonsurgical treatments exist for many of these issues, but surgery remains the most effective therapy. Because of the considerable sensory innervations of the canal of anal, patients feel substantial discomfort during anorectal surgery [2]. Sensitization of both peripheral and central pain receptors is hypothesized to have a role in postoperative pain [3]. After excisional hemorrhoidectomy, two types of pain are identified that is rest discomfort and defecation pain. Most of the patients have rest discomfort, which happens without any effort of defecation or straining. It is generally the most intense in the first 24 hours after excisional hemorrhoidectomy, then progressively fades after that beginning on the 2nd postoperative day. Defecation pain occurs when the anal wound is irritated by fecal waste and the internal anal sphincter IAS spasms during or after defecation. On the 2nd postoperative day, patients generally feel defecation discomfort, which is the 2nd peak of anal pain following the 1st peak (rest pain) that subsided [4]. according to Ho et al., Many patients would rather live with their previous hemorrhoidal problems than suffer postoperative discomfort. Proctologists are divided into preoperative and postoperative proctologists in an attempt to reduce it, however, there is no agreement or unified standards in this area [5]. The most common treatment for a perianal abscess is surgery in a clinic. Nevertheless, the most common concern in postoperative patients is a discomfort caused by dressings, and the number of analgesics accessible is restricted [6]. Patients having anorectal surgery should be given a multimodal analgesic regimen that includes oral analgesic, paracetamol, nonsteroidal anti-inflammatory medications (NSAIDs), and opioids, as well as topical anesthetics, ointment laxatives, and oral metronidazole, according to a recent study [7].

Methods

PubMed, Embase, Medline, Science Gate, Scientific Report, Elsevier, Google Scholar, and Cochrane Evidence-Based Medicine Reviews were used to conduct a review search. Review of newly released books and papers with regard to the topic, as well as manual searches (Comparison of various analgesic protocols for control of postoperative pain following anorectal surgery), was started at (May,2021). we searched, the published studies from 2011 to the present date by the full text:(various analgesic protocols post anorectal surgery).

Including Criteria: All available articles related to the research keywords and identified topic related to analgesic protocols post anorectal surgery.

Exclusion Criteria: Articles that do not adjust to the topic, all articles which are not open access. All articles that were not translated to the English language all articles published or unpublished before 2011, age below 18 years, and pregnancy.

Postoperative pain: As per the "International Association for the Study of Pain", an uncomfortable emotional feeling accompanying with actual or potential injury, or described in terms of such harm. Because of the possible deleterious consequences of the physiologic response to pain following surgery, effective management and control of postoperative pain are obviously of main concern to the patients and also of relevance to the surgeon. Inadequate postoperative pain care remains a significant clinical issue, resulting in not only poor immediate postoperative results but also a higher risk of long-term postoperative discomfort [8]. Chronic discomfort following anorectal surgery can be caused by a variety of factors. Remaining underlying disease, new or persistent fissure and/or thrombosed hemorrhoids, or subtle anal infection can all cause this pain. If the patient's postoperative discomfort lasts longer than expected, a thorough examination must be done to rule out the abovementioned reasons, with specific attention devoted to the likelihood of a hidden infection or a nonhealing wound [9]. The specific origin of pain following excisional hemorrhoidectomy is unknown, however it appears to be complex. Several explanations have been presented to explain the discomfort experienced after a hemorrhoidectomy. Other contributory variables include the insertion of the anal pack, damage to the nerve ending or the anal canal mucosal lining, suturing at the pedicle or below the dentate line, wound infections, and the formation of anal fissures [4]. Pain is presently measured using a variety of pain assessment measures. The category intensity rating scale, the "numeric pain intensity rating scale, the Wong-Baker face intensity scale", and the visual analog scale are some examples of such measures [10].

The most common methods preventing or reducing pain after anorectal surgery include:

wound infiltration. Local anesthesia can be achieved by infiltrating lidocaine or bupivacaine into the wound. The effects of epinephrine are immediate following subcutaneous or intradermal delivery, and it extends anesthesia duration [8]. The amount of local anesthetics necessary is determined by the size of the region to be anesthetized and the length of time the process is estimated to take. When compared to placebo/routine analgesia, local anesthetics wound infiltration methods lowered opioids needs and pain ratings, and enhanced recovery in patient undergoing colorectal Postoperative Pain Control 307 surgery [11]. After local infiltration with ropivacaine vs. isotonic saline during hemorrhoidectomy, Vinson et al identified a significant difference in pain levels in the immediate postoperative phase [7].

Pudendal nerve block pudendal nerve is a sensory nerve that arises from the S2-4 nerve root. The external urethral and external anal sphincter are innervated by motor fibers in this area. The inferior rectal, peroneal, and dorsal nerves of the penis/clitoris are all branches of the pudendal nerve. The skin around the anus is innervated by the first branch (which exits the nerve right before or within Alcoks canal). The medial and lateral labial (scrotal) branche have a deep motor part and 2 sensory sections. The third branch, which innervates the overlaying skin, goes along the skin of the penis/clitoris. perineal discomfort is a debilitating ailment that causes pain along the anatomical distribution of the nerve, is increased by sitting, and does not wake the patient up at night if caused by an afflicted pudendal [12]. Pudendal nerve block (PNB) combined with Spinal anesthesia that used for hemorrhoidectomy in recent years, and it has been shown to reduce postoperative discomfort [13]. Pudendal nerve block is generally administered bilaterally for improved postoperative relief. When levobupivacaine 0.25 percent or 0.5 percent is used bilaterally, the analgesic influence continues for several hours without any need for relief or rescue analgesia, resulting in less discomfort and increased patient comfort when defecation happens on the day of the surgery [10].

Causal epidural analgesia: is a tried-and-true methods of controlling postoperative pain that has been around for decades at a stretch. According to studies, the approach provides a number of other advantages, including reduced cardiovascular, pulmonary, and gastrointestinal morbidity [14]. Caudal anaesthesia is a low-cost and simple procedure. Sicard and Cathelin disclosed caudal anaesthesia for minor anorectal surgery for the first time in 1990 Because of the fear of pre- and postoperative chronic pain, surgeons have been hesitant to perform rectal and anal procedures under caudal anaesthesia. Caudal block involves placing a needle through the sacral hiatus into the epidural region to provide medicine. This method is also used in a widely range in the treatment of people suffering from chronic pain. Local anaesthesia has a number of advantages, including a reduction in patient recovery time, a reduction of nursing care for postanaesthesia, and a reduction in the amount of analgesic required in the immediate postoperative period [15].

Transcutaneous electrical nerve stimulation (TENS):

A high frequency electrical current to the skin's surface. TENS' analgesic effect is transmitted by a variety of methods, according to the kind of stimulation used. Transcutaneous electrical nerve stimulations with low strength (5-10 mA) and high frequency (10-200 Hz) provides a strong and pleasurable paresthesia feeling and activates the big myelinated alpha, beta (Ab) fiber, controlling pain at the spinal cord level via the gate control hypothesis [16-17]. Chiu et al. compared 30 patient that got Transcutaneous electrical nerve stimulations following excisional hemorrhoidectomy to an equivalent number of patients who did not get Transcutaneous electrical nerve stimulations in a randomized trial. Up to 24 hours, the TENS group had considerably lower particular pain score and required much less morphine than the control group. It could be due to the enhanced release of endogenous morphine [4]. Technical tips:

The ligasure vessel closing system was recently released as an instrument designed to improve the standard treatment of haemorrhoid: it involves of a bipolar electro thermal devices that delivers an optimized mixture of pressure and radio- frequency, closing blood vessels up to seven mm in diameter and producing energy matched to tissues impedance, with a thermal damage restricted to two mm above the surgical location. Because of the restricted spread, anal spasm is decreased, allowing for a bloodless haemorrhoidectomy with less postoperative discomfort and faster recovery [18].

Bipolar electrothermal The cautery's power is set to 40W. The haemorrhoidal bundle is gently dissected from the internal sphincter, up to the pedicle at the anorectal ring, after a skin incision is made with bipolar diathermy scissors. The bipolar electro thermal devices are new hemostatic devices that can provide a precise quantity of electro cautery energy through vascular structure with minimum thermal dispersion in the surrounding area. Bipolar diathermy haemorrhoidectomy that found to minimize operating time and postoperative discomfort [19].

Harmonic Scalpel: an ultrasonically actuated tool that shakes at a speed of 55,000 times per second and is powered by sound waves. It's renowned for its capacity to coagulate tiny and medium-sized vessel, therefore it might help to reduce swelling and edema in the surrounding tissue after surgery. 5 The Harmonic Scalpel has the distinct benefit of producing very minimal tissue damage. Reduced postoperative discomfort is associated with a smaller surgical site damage (1.5 mm). 8 Harmonic scalpels have been discovered to provide several advantages in various surgeries, including smaller incisions, shorter hospital stay, less tissue damage, faster healing, and decreased scarring [19].

Warm Water baths: non- sterile medical gloves were occupied with water at (40°C) and utilized for the study

procedure. Warm plastic bag used to the perianal area 4 time with 15-minute per session 2 hours after weaning from the effect of spinal anesthetic for post- operative pain control following hemorrhoidectomy are routinely used for pain control as a safe approach with comparatively reduced morbidity. Likewise, the same approach is used to decrease discomfort and improve recovery following some gynecological and urological operations. Warm water bath that linked to internal anal sphincter relaxation, resulting in pain relief and continuous relaxation [20].

Most systemic and topical agent:

Topical nitrates Since the discovery of NO (nitricoxide) as an inhibitor of IAS (internal anal sphincter) tone, nitrates have been found to diminish anal hypertonia and have been the first-line treatment for chronic anal fissures in many clinical settings [21]. Topical administration of nitroglycerin lowers the internal anal sphincter in normal human patients, according to Loder et al. and Guillemot et al. As a result, it was widely assumed that Glyceryl trinitrate (GTN) and others nitrates may alleviate pain by relaxing the internal anal sphincter [22].

Botolinium toxin Clostridium botulinum is an anaerobic bacterium that generates toxins that target presynaptic nerve terminals. Injections of botulinum toxin resulted in a considerable reduction in anal resting pressure of 18 to 30 percent in studies. When administered into the external anal sphincter, Patti's study found that therapy with botulinum toxin successfully reduced material requirements planning (MRP) levels as well as postoperative discomfort, both when resting and during defecation [22].

Diltiazem. A benzothiazepine is an L-type calcium channel antagonist works by preventing extracellular calcium ions from entering the human internal anal sphincter sarcoplasm which saves oxygen and causes muscular relaxation and pain alleviation. diltiazem ointment is statistically significant in lowering postoperative pain: less than 48 hours, 72 hours, and 96 hours or more. The 2 percent diltiazem-ointment provided postoperative pain alleviation for the majority of the patient [23].

Methelyne blue (MB) is a biological stain that is commonly used. The usage of highly concentrated topical MB in anorectal surgery not only stains the tip and nerve fiber, but also temporarily disrupts their role. To the best of our knowledge, MB has been used to cure neuritis, relieve pruritus, and provide analgesia during anorectal surgery [24-26]. Perianal intradermal injection gives short pain alleviation following hemorrhoidectomy and lateral anal sphincterotomy, according to studies conducted in Singapore and China. Other investigations found that injecting MB intradermal into participants with severe anal pruritus (intractable anal pruritus) improved their symptom score [26-27].

Policresulene and Cinchocaine:

Policresulene: The association's major component is an organic acid with a large molecular weight, an ionic potential hydrogen (pH) of 4, and a half-life of 4-5 hrs. It has hemostatic properties by forcing blood protein to coagulate and stimulating the contractions of the fibers of muscle of tiny blood vessel. cinchocaine The amide group topical anesthetic is similar to mepivacaine, lidocaine, prilocaine, and bupivacaine, but differs by its lipophilic moiety having a double aromatic ring. It has a quick action time of around 15 min, with a peak activity time of 2-4 hours. Patients and clinicians agree that the mixture of topical cinchocaine and policresulen, without the adding of corticosteroid or antibiotic, is effective in the clinical management of hemorrhoid and, more controversially, in postoperative care [5].

Diclofenac and EML A cream: is the most often prescribed non- steroidal anti- inflammatory drugs (NSAID) in the world [28]. Analgesic, antibacterial and anti-inflammatory, properties are shared by lidocaine and diclofenac. These features are appropriate for treating three types of post- operative pain in (benign anorectal surgery) BARS: inflammatory, nociceptive (visceral and somatic), and pain caused by super- infection of the dirty region. The topical EMLA cream, that comprises 2.5 % lidocaine and 2.5 % prilocaine, is one of the most regularly used chemicals to induce regional anesthesia. In patients having hemorrhoidectomy, it appears that its use is linked to less post-surgical discomfort and less narcotic administration Diclofenac suppositories have been shown to relieve and decrease postsurgical pain in a variety of surgeries (Rahimi et al., 2012) [29].

The Vitamin E has also been found to have an antiinflammatory impact on dermatological illnesses, lowering edema and moderating the rise of cyclooxygenase-2 (COX-2), the enzyme that catalyze the manufacture of prostaglandin E2, which play a role in the local inflammatory response. vitamin E lowers postoperative discomfort after skin wound and hemorrhoidectomy [30].

Cholestyramine is a bile acid sequestrant that binds to bile acid in the colon and produces a non-absorbable compound. As a results, it inhibits the enterohepatic reuptake of intestinal bile salt, resulting in a reduction in low-density lipoprotein and total plasma cholesterol. Cholestyramine has also been discovered to have some other functions. Because bile acid irritates the skin and cholestyramine inhibits the formation of bile salt, a topical medicine was used in several research to minimize the inflammatory effect of these acid. Pain after hemorrhoidectomy, irritating diaper dermatitis, perianal skin irritation after ileoanal anastomosis, skin irritation surrounding enterostomies, biliary fistulas, perianal irritation, and diaper rash are among the documented side effects [31].

Baclofen: GABA-B receptors are numerous in the CNS; baclofen is a stereospecific agonist at these receptors [32]. In recent times administered baclofen cream 5 percent to patient who had open hemorrhoidectomy for the purpose of reducing postoperative pain, and maintained the treatment every 12 hours for 14 days. From the first week onwards, VAS (Visual Analog Scale) results revealed substantial differences between the treatment and placebo group in postoperative pain levels. Furthermore, individuals using baclofen did not require the usage of other analgesics [33]. Sucralfate in mild acidic conditions, the basic aluminum salt of sucrose octasulfate dissociates. It absorbs bile salt and creates insoluble adherent complexes on the site, protecting it from mechanical injury and preventing the release of inflammatory cytokine from injured epithelial cell, inducing in pain relief [34]. Gupta et al. found that topical treatment of 3 grams sucralfate improved discomfort following hemorrhoidectomy and lowered analgesic needs, notably after seven to fourteen days [35].

Pain management by using antibiotics:

Metronidazole in 1950, it was found, and in 1957, it was synthesized. This is a broad-spectrum antibiotic used to treat anaerobic infections and protozoan protozoans. It belongs to the nitroimidazole class of antibiotics in the field of proctology, it is used in conjunction with other antibiotics to treat anaerobic bacteria infections, depending on the degree and severity of the damage. Antibiotics like metronidazole help minimize bacterial growth, inflammation, and post- operative discomfort, which is not unexpected given that bacterial colonization is unavoidable following hemorrhoidectomy [36].

Reducing pain by using opioids:

Tramadol is a synthetic opioid that works as an agonist on opioid-receptors. It also prevents norepinephrine and serotonin from being reabsorbed. Its primary application is in the treatment of mild to moderate pain. Tramadol cannot be regarded the medicine of choice for moderate to severe acute pain when used alone for a subgroup of patients, such as those having excisional hemorrhoidectomy or those with extensive wounds [37].

Fentanyl is a totally synthetic opioid that stimulates receptors. It was the first opioid in the fentanyl family, which eventually included sufentanil, alfentanil, and remifentanil for human patients and carfentanil and thiofentanil for wild animals. The beginning of action and peak plasma concentrations of fentanyl are dependent on the dose and administration mode employed. Analgesia can start as quickly as 1-2 mins after intravenous fentanyl injection, but most buccal trans mucosal delivery techniques take 10 to 15 minutes [38]. Bupivacaine 5 mg with fentanyl 15 g for anorectal surgery had a better mean numeric rating scale score in the first six hours. Early postoperative pain can be relieved with 0.3 intrathecal fentanyl, which can also reduce the likelihood of rebound pain as the block's effect wears off [39].

Morphine and Oxycodone:

Morphine is the most common opioid agonist and the gold standard for treating acute pain. It has a moderate analgesic effectiveness, a slow onset, and a mid-length of action [40]. Following excisional hemorrhoidectomy, Goldstein and colleagues20 found that 21 of 22 patients who used a subcutaneous morphine pump had adequate pain management. The authors classified the subcutaneous morphine pump as a cost-effective approach for pain control after excisional hemorrhoidectomy [4].

Oxycodone is an opioid agonist that is broken down in the liver. Oxycodone was shown to be more effective than morphine in an experimental pain model for pain caused by mechanical and thermal stimulation of the esophagus, indicating that it might be more efficacious than morphine in visceral pain [8].

Ketamine:

Ketamine is a drug that may be taken orally, rectally, nasally, intravenously, intramuscularly, epidurally, or intrathecally. Ketamine also has the majority of the features of a perfect anesthetic, such as a dose-dependent analgesic effect, amnesia, unconsciousness, stress suppression, and akinesia [41]. Its topical treatment for localized neuropathic pain depends on a non-competitive N-methyl-D-aspartic receptor blockage, and pain modulation is accomplished by inhibiting glutamate synthesis [42]. Local infiltration and block are two painrelieving procedures used in anorectal operations. Lidocaine, ropivacaine, or a mixture of lidocaine and bupivacaine, with or without adrenaline, have all been proposed as local anesthetics. Many research has looked at the effects of combining local anesthetics with local ketamine injections [43].

Pain management: by method of surgery Due to a reflex spasm of the internal anal sphincter, anorectal surgery is accompanied with significant postoperative pain. Pain relief after a hemorrhoidectomy has been attempted using a variety of ways. Lateral internal sphincterotomy has really been accepted as a legitimate complement to hemorrhoidectomy for improved postoperative pain management over time. By lowering the hypertonicity of sphincter, lateral the internal anal internal relieves post-hemorrhoidectomy sphincterotomy discomfort [44]. Asfar et al found that performing an internal sphincterotomy via one of the hemorrhoidectomy sites on a regular basis considerably lowers posthemorrhoidectomy discomfort and problems [45].

Multimodal analgesia: The multimodal approach is the best treatment strategy for a patient's post-surgical discomfort. The physician can design a customised treatment plan that takes into consideration the patient's personal and medical needs by combining the drugs and strategies outlined in this article. Multimodal pain treatment includes the use of several pharmacologic modes of action, as well as additive or synergistic effects, that operate on various locations within the central and peripheral nervous systems. to offer appropriate pain management, reduce the quantity of opioids necessary after surgery, and thereby reduce the side effects associated with them [8].

Results

Anorectal surgery is marked by excruciating discomfort following the procedure. Using the new technique throughout anorectal surgery as hemorrhoidectomy to avoid more excision of the skin and anal mucosa, putting the sutures proximal to the dentate line and away from the internal anal sphincter IAS, and good hemostasis to avoid inserting of anal pack are the most important methods to reduce pain postoperatively, regardless of the type of anorectal surgery. performed or the instrument used during it. We can categorize what we've discovered. Different sets of research have recently embraced pain management following anorectal surgery. We found more protocols using multimodality pain management for pain relief such as, topical drugs that produce direct relaxation of the internal anal sphincter, topical intervention as a pudendal nerve block, a method of surgery as surgical sphincterotomy and technical tips to reduce pain as ligasure.

Conclusion

The goal of this study was to search through the current literature to find the most practical and successful techniques in this situation. Because of the various causes of discomfort in many types of surgery, multimodal pain treatment has been found to minimize pain intensity and narcotic usage. According to the highest degree of proof, using current technological procedures and tools as a ligasure with some topical agent as GTN glyceryl trinitrate ointment provided amazing good alleviation of postoperative pain following anorectal surgery as excisional hemorrhoidectomy. There isn't enough information to say that pain can be fully eliminated. More research and development of current procedures are required to entirely eliminate the patient's discomfort following anorectal surgery.

Caution

we can't prevent using opioids post anorectal surgery but we can decrease its consumption by giving a asmall dose of it to prevent complication. The use of analgesic protocols must not be given randomly but according to the patient's response and pain score.

References

- [1] Gorfine SR, Onel E, Patou G, Krivokapic Z V. 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(12):1552–9.
- [2] Leinicke JA, Carbajal V, Senders ZJ, Patil N, Wogsland A, Stein SL, et al. Opioid Prescribing Patterns After Anorectal Surgery. J Surg Res. 2020; 255:632–40.
- [3] Van Backer JT, Jordan MR, Leahy DT, Moore JS, Callas P, Dominick T, et al. Preemptive analgesia decreases pain following anorectal surgery: A prospective, randomized, double-blinded, placebocontrolled trial. Dis Colon Rectum. 2018;61(7):824– 9.
- [4] Emile SH. Evidence-based review of methods used to reduce pain after excisional hemorrhoidectomy. J Coloproctology [Internet]. 2019; 39(1):81–9.
- [5] Froehner Junior I, Kotze PG, Rocha JG, Miranda EF, Sartor MC, Martins JF, et al. Analgesia tópica com policresuleno e cinchocaína no pós-operatório de hemorroidectomias: Um estudo prospectivo e controlado. Rev Col Bras Cir. 2014;41(2):92–8.
- [6] Zhang JJ, Gao HX, Zhang TT, Bao WQ, Mou JY, Meng K, et al. Pre-mixed nitrous oxide/oxygen mixture treatment of pain induced by postoperative dressing change for perianal abscess: Study protocol for a randomized, controlled trial. J Adv Nurs. 2020; 76(12):3623-30.
- [7] Ceulemans A, De Looze D, Van de putte D, Stiers E, Coppens M. High post-operative pain scores despite multimodal analgesia in ambulatory anorectal surgery: a prospective cohort study. Acta Chir Belg. 2019; 119(4):224-230.
- [8] Lovich-Sapola J, Smith CE, Brandt CP. Postoperative Pain Control. Surg Clin North Am. 2015; 95(2):301– 18.
- [9] Kunitake H, Poylin V. Complications Following Anorectal Surgery. Clin Colon Rectal Surg. 2016; 29(1):14–21.
- [10] Iranpour A, Boddapati R, Vranken JH. Multimodality post proctologic surgery pain control. Semin Colon Rectal Surg. 2019; 30(4):100701.
- [11] Ventham NT, O'Neill S, Johns N, Brady RR, Fearon KCH. Evaluation of novel local anesthetic wound infiltration techniques for postoperative pain following colorectal resection surgery: a metaanalysis. Dis colon rectum. 2014; 57(2):237–50.
- [12] Richard III HM, Marvel RP. CT guided pudendal nerve block. Open J Radiol. 2013; 03(01):41-44.
- [13] He J, Zhang L, Li DL, He WY, Xiong QM, Zheng XQ, et al. Ultrasound-Guided Pudendal Nerve Block Combined with Propofol Deep Sedation versus

Spinal Anesthesia for Hemorrhoidectomy: A Prospective Randomized Study. Pain Res Manag. 2021; 2021.

- [14] Rawal N. Epidural technique for postoperative pain: Gold standard no more? Reg Anesth Pain Med. 2012; 37(3):310–7.
- [15] Malik S, Mirani SH, Kumar D. Effectiveness of Caudal Epidural Anaesthesia in Anorectal Surgery. Prof Med J. 2019; 26(07):1121–4.
- [16] Coutaux A. Non-pharmacological treatments for pain relief: TENS and acupuncture. Jt Bone Spine. 2017; 84(6):657–61.
- [17] Claydon LS, Chesterton LS, Barlas P, Sim J. Dosespecific effects of transcutaneous electrical nerve stimulation (TENS) on experimental pain: a systematic review. Clin J Pain. 2011; 27(7):635–47.
- [18] Gentile M, De Rosa M, Carbone G, Pilone V, Mosella F, Forestieri P. LigaSure Haemorrhoidectomy versus Conventional Diathermy for IV-Degree Haemorrhoids: Is It the Treatment of Choice? A Randomized, Clinical Trial. ISRN Gastroenterol. 2011; 2011:1–6.
- [19] Sarkar A, Choksi DB, Sutaria A, Sindhal M. Harmonic scalpel versus bipolar diathermy in Milligan-Morgan haemorrhoidectomy: a randomized controlled study. Int Surg J. 2018; 5(7):2507.
- [20] Altomare DF, Giannini I. Pharmacological treatment of hemorrhoids: A narrative review. Expert Opin Pharmacother. 2013; 14(17):2343–9.
- [21] Altomare DF, Binda GA, Canuti S, Landolfi V, Trompetto M, Villani RD. The management of patients with primary chronic anal fissure: A position paper. Tech Coloproctol. 2011; 15(2):135–41.
- [22] Uzzaman MM, Siddiqui MRS. A brief literature review on the management of posthaemorrhoidectomy pain. Surg Tech Dev. 2011; 1(2):e32.
- [23] Huang YJ, Chen CY, Chen RJ, Kang YN, Wei PL. Topical diltiazem ointment in posthemorrhoidectomy pain relief: A meta-analysis of randomized controlled trials. Asian J Surg. 2018; 41(5):431-437.
- [24] Sim H, Tan K. Randomized single-blind clinical trial of intradermal methylene blue on pain reduction after open diathermy haemorrhoidectomy. Color Dis. 2014; 16(8):O283–7.
- [25] Oz M, Lorke DE, Hasan M, Petroianu GA. Cellular and molecular actions of methylene blue in the nervous system. Med Res Rev. 2011; 31(1):93–117.
- [26] Fransiska D, Jeo WS, Moenadjat Y, Friska D. Methylene Blue Effectiveness as Local Analgesic after Anorectal Surgery: A Literature Review. Adv Med. 2017; 2017:1–5.
- [27] Samalavicius NE, Poskus T, Gupta RK, Lunevicius R. Long-term results of single intradermal 1% methylene blue injection for intractable idiopathic pruritus ani: a prospective study. Tech Coloproctol. 2012; 16(4):295–9.
- [28] McGettigan P, Henry D. Use of non-steroidal anti-

inflammatory drugs that elevate cardiovascular risk: an examination of sales and essential medicines lists in low-, middle-, and high-income countries. PLoS Med. 2013; 10(2):e1001388.

- [29] Rahimi R, Abdollahi M. A systematic review of the topical drugs for post 64. Bou Ghanem EN, Clark S, Du X, Wu D, Camilli A, Leong JM, et al. The α-Tocopherol Form of Vitamin E Reverses Age-Associated Susceptibility to Streptococcus pneumoniae Lung Infection by Modulating Pulmonary Neutrophil Recruitment. J Immunol. 2015; 194(3):1090–9.
- [30] Ruiz-Tovar J, Garcia A, Ferrigni C, Duran M. Application of Vitamin E Acetate on Staple Lines and Anastomoses of Roux-en-Y Gastric Bypass: Impact on Postoperative Pain and Acute Phase Reactants. Obes Surg. 2020; 30(8):2988–93.
- [31] Ala S, Alvandipour M, Saeedi M, Seyedein S, Monajati M, Koulaeinejad N. Evaluation of Cholestyramine 15% Ointment in Relieving Pruritus and Burning After Ileostomy: A Rrandomized, Double-Blind Placebo-Controlled Clinical Trial. J Investig Surg. 2020;33(9):795–802.
- [32] Whitehead RA, Puil E, Ries CR, Schwarz SKW, Wall RA, Cooke JE, et al. GABAB receptor-mediated selective peripheral analgesia by the nonproteinogenic amino acid, isovaline. Neuroscience. 2012; 213:154–60.
- [33] Nemeth BA, Montero RJ, Halanski MA, Noonan KJ. Epidural baclofen for the management of postoperative pain in children with cerebral palsy. J Pediatr Orthop. 2015; 35(6):571–5.
- [34] 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(1):233–8.
- [35] Uzzaman MM, Siddiqui MRS. A brief literature review on the management of posthaemorrhoidectomy pain. Surg Tech Dev. 2011; 1(2):e32.
- [36] 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 Enfermedades Dig. 2015; 107(11):681-5.
- [37] Iranpour A, Boddapati R. Multimodality post proctologic surgery pain control. In: Seminars in Colon and Rectal Surgery. Elsevier; 2019. p. 100701.
- [38] Honca M, Dereli N, Kose EA, Honca T, Kutuk S, Unal SS, et al. Low-dose levobupivacaine plus fentanyl combination for spinal anesthesia in anorectal surgery. Braz J Anesthesiol. 2015; 65(6):461-5.
- [39] Shim SM, Park JH, Hyun DM, Jeong EK, Kim SS, Lee HM. The effects of adjuvant intrathecal fentanyl

on postoperative pain and rebound pain for anorectal surgery under saddle anesthesia. Korean J Anesthesiol. 2018;71(3):213–9.

- [40] Gandhi K, Baratta JL, Heitz JW, Schwenk ES, Vaghari B, Viscusi ER. Acute pain management in the postanesthesia care unit. Anesthesiol Clin. 2012; 30(3):e1–15.
- [41] Periodicals W. Does Ketamine Improve Postoperative Analgesia? More Questions Than Answers. 2011;1135–6.
- [42] Casale R, Symeonidou Z, Bartolo M. Topical Treatments for Localized Neuropathic Pain. Curr Pain Headache Rep. 2017;21(3):15.
- [43] Kazemeini A, Rahimi M, Fazeli MS, Mirjafari SA, Ghaderi H, Fani K, et al. The effect of local injections

of bupivacaine plus ketamine, bupivacaine alone, and placebo on reducing postoperative anal fistula pain: A randomized clinical trial. Sci World J. 2014; 2014:4–9.

- [44] Farooq AS, Ahmed S, Javed MR, Rizwan S, Asif M, Khan RH. Comparison of Hemorrhoidectomy alone Vs Hemorrhoidectomy with Lateral Sphincterotomy in Terms of Post-Operative Pain Relief. Hemorrhoidectomy alone Vs Hemorrhoidectomy. 2019; 13(4):283-6.
- [45] DK Das U. Effectiveness of Internal Sphincterotomy in reducing Post Open Hemorrhoidectomy Pain: A Randomized Comparative Clinical Study. Int J Collab Res Intern Med Public Heal. 2013; 5(6):428– 35.