Journal of Lasers in Medical Sciences

J Lasers Med Sci 2024;15:e52

Original Article

http://journals.sbmu.ac.ir/jlms

doi 10.34172/jlms.2024.52

High-Intensity Laser Therapy – An Option for Managing the Pain in Anal Fissures

Sônia Cristina Cordeiro Time[1,2,3*], Ana Carolina Buffara Blitzkow[4,3], Fabrício Doin Paz de Oliveira[5,3], Luana Perondi[6], Elisa Treptow Marques[3], Abel Botelho Quaresma[6], Marcelo Marciano[7], Rodnei Bertazzo Sampietro[5,3]

[1]Coloproctology Department, Hospital Santa Cruz rede Do'r, Curitiba, Paraná, Brazil
[2]Coloproctology Department, Vita Batel Hospital, Curitiba, Paraná, Brazil
[3]Academia do Laser (ADL) Concordia, Santa Catarina, Brazil
[4]General and Digestive Surgery Department, Santa Cruz Hospital – rede Do'r Hospital, Curitiba, Paraná, Brazil
[5]Center for Inflammatory Bowel Diseases and Coloproctology- Sao Camilo Hospital, Concordia, Santa Catarina, Brazil
[6]UNOESC, Medicine Faculty, Center of Inflammatory Bowel Diseases and Coloproctology, Joaçaba, SC, Brazil
[7]Santa Casa de Misericórdia de Votuporanga - Votuporanga, SP , Brazil

***Correspondence to**
Sônia Cristina Cordeiro Time,
Email: sonia.time@gmail.com

Received: June 18, 2024
Accepted: September 11, 2024
ePublished: October 23, 2024

Abstract

Introduction: Anal fissures (AFs) are a prevalent pathology. Although internal lateral sphincterotomy is still the gold-standard surgery for treating chronic AFs, this procedure is associated with a considerable risk of anal incontinence. This study describes an alternative and minimally invasive technique for treating AFs using photobiomodulation and a high-power diode laser-fissure treatment (LFT) and highlights initial results pertaining to pain.

Methods: This retrospective study focused on 38 patients treated with LFT on an outpatient basis at three different hospitals in different states of Brazil (Santa Catarina, Paraná, and São Paulo). The objective was to evaluate the effects of LFT treatment on AF patient pain following the procedure. The Friedman test was used to identify the effects of LFT treatment over time (D0, D7, D15, D30, and D60) on postoperative pain intensity using the visual analogue scale (VAS). Complications and incontinence rates were also analyzed.

Results: Roughly two-thirds of the patients (66%; n=25) were male. The median age of the cohort was 49. Constipation was described by 32% of the patients, 13% were smokers, and 21% had recently used opioids. In 92% of the cases, the AF was localized posteriorly. Skin tags were present in 27% of the cases, and 26% had recently undergone a previous orificial surgery. A significant reduction in pain was observed over time in the intensity of postoperative pain measured by the VAS. Prior to surgery (D0), the patients' mean VAS score was 4.1; it progressively decreased to 0.1 on the 60th postoperative day ($P<0.05$). There was no significant change in fecal continence at the end of the 60-day follow-up period. Minor complications occurred in 7.9% of the patients (2.6% hemorrhoidal thrombosis, 2.6% skin tag, and 2.6% "failure").

Conclusion: Our results suggest that treating AFs with laser therapy results in a significant reduction in pain intensity over time without interfering with anal continence.

Keywords: Fissure-in-ano; Low-level light therapy; Laser therapy; Colorectal surgery.

Introduction

Anal fissures (AFs), or fissures-in-ano, are a prevalent pathology in proctology. With a lifetime incidence of 7.8% and approximately 350 000 new cases di60 agnosed each year in the United States, this condition requires effective treatment.[1-3]

The most common symptom of AFs is intense and debilitating anal pain during evacuation.[4,5] Although most AFs are healed by conservative means, there is a significant proportion of fissures that become chronic and can negatively impact a patient's quality of life.[6-9]

The treatment of acute fissures is aimed at relieving pain, reducing anal spasms, and healing tissue. Conservative management with stool softening and analgesia is typically the first course of treatment.[4] Glyceryl trinitrate, topical diltiazem, and nifedipine can be attempted to reduce pain and anal spasms. In cases of chronic disease, local injections of botulinum toxin or surgical interventions, such as lateral intern sphincterotomy for definitive management, may be considered when conservative therapy fails. However, surgical treatment still carries with it a considerable risk of fecal incontinence.[1,4,5-10]

In recent years, new procedures have been proposed for treating AFs without injuring the anal sphincter.[11-13]

Please cite this article as follows: Time SCC, Blitzkow ACB, Oliveira FDPd, Perondi L, Marques ET, Quaresma AB, et al. High-intensity laser therapy – an option for managing the pain in anal fissures. *J Lasers Med Sci.* 2024;15:e52. doi:10.34172/jlms.2024.52.

Minimally invasive laser energy methods are emerging and becoming more prominent in the literature.[14-17] This study describes photobiomodulation for AFs using a high-power laser. This technique is an example of laser-fissure treatment (LFT). We focused on pain relief in the case of both acute and chronic AFs. This study has focused on the pain since this symptom in Afs is usually intense and can be debilitating.[18]

Methods

This retrospective study was conducted with patients treated with LFT between March 2019 and February 2024. The study was approved by the Research Ethics Committee of the Universidade do Oeste de Santa Catarina, UNOESC ("Plataforma Brasil" 63897722.9.0000.5367). Three colorectal surgeons performed outpatient treatment on 38 patients at three hospitals in different states in Brazil (Santa Catarina, Paraná, and São Paulo).

All of the patients were older than 18 years and had AFs detected upon physical examination. Those fissures could be acute, chronic, or postoperative; pain, localized in the anterior or posterior medical line, was the patients' leading complaint. All of the patients included in this study underwent a high-power laser treatment session. The treatment proposal was offered by an attending coloproctologist and accepted by each patient.

Patients with anal fistulas, inflammatory bowel disease, malignancy, infectious diseases, diagnosed sexually transmitted infections, or fissures located not on the anterior or posterior midline were excluded from this investigation.

Although this study was carried out in a multicentric manner, our approach was still standardized. We focused on a group of surgeons who all trained in laser coloproctological surgery at the same educational institution. These individuals also currently serve as the teaching staff of that institution. The same laser parameters were used in all of the surgeries.

A diode laser (Neo-V, Neolaser, Israel) with a flat probe operating at a wavelength of 1470 nm with a 600-µm fiber and 1–2 W of power was applied intraoperatively 3 mm above the lesion. The scanning method involved a fluency of up to 30 J/cm^2. Figure 1 shows images of the procedure and the appearance of AF on D0 and D14.

During the postoperative period, the patients were given ketorolac (10 mg, sublingually), three doses per day, for pain management. Dipyrone (1 g, orally) was also given the first three days postoperatively.

All patients were contacted 7, 15, 30, 60, 90, and 180 days (by face-to-face consultation or telephone) after their procedure. Epidemiological data, smoking status, medication use, and information about previous constipation from the patient's medical records were collected. The primary objective of this study was to evaluate pain intensity using the visual analogue scale (VAS).

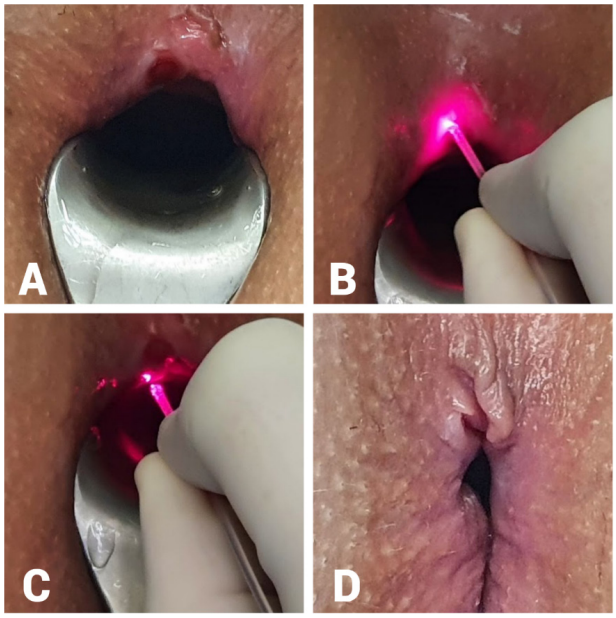

Figure 1. Panel A: Anal fissure prior to treatment; Panels B and C: Laser Photobiomodulation (LFT); Panel D: Anal Fissure 14 Days After Treatment

0	1	2	3	4	5	6	7	8	9	10
No pain										Worst pain

Figure 2. Visual Analog Scale

The VAS is a proven subjective tool for measuring pain.[19] Users select a value on a continuum between 0 and 10, corresponding to "no pain" and "worst pain" (Figure 2).[19]

In addition, healing (i.e., the absence of the previous wound in the anoderm), recurrence (i.e., the return of symptoms and lesions within 90 days), and alterations in anal continence were recorded. The Wexner Score (the Cleveland Clinic Fecal Incontinence Severity Scoring System; CCIS) was used to measure fecal incontinence. The Wexner Score ranges from 0–20, where 0 is perfect continence and 20 is complete incontinence (Table 1). [20] Complications were also classified and detailed by using the Clavien-Dindo system.[21]

Statistical Analysis

A Friedman test was employed to compare changes in the VAS scores over time. Dunn-Bonferroni post hoc tests were also used to evaluate the differences between scores and baseline values. The significance level was set at 0.05. IBM SPSS Statistics for Windows (version 21.0, Armonk, NY, USA) was used for the analyses.

Results

Table 2 lists the sample characteristics and demographics. Of the patients, 26% had recently undergone orificial surgery. Hemorrhoidectomy was the most common

Table 1. Wexner Score[20]

Type of incontinence	Frequency				
	Never	Rarely	Sometimes	Usually	Always
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wear pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

procedure (n = 4), followed by fistulectomy (n = 3), rubber band ligation (n = 1), bowel transit reconstruction (n = 1), and fistulotomy (n = 1). The mean duration of patients' symptoms was 19 months (range: 1–144 months; Table 2).

The patients' VAS scores were compared over time, and we investigated how they evolved from D0 (baseline) (Table 3). A progressive decrease in the mean score was noted over time. The Friedman test revealed a significant difference over time ($\chi^2 = 109.078$, df = 4, $P < 0.0001$). Dunn-Bonferroni multiple comparisons showed a significant difference at all times compared with the baseline ($P < 0.05$). Prior to surgery (D0), the mean VAS was 4.1; it progressively decreased to 0.1 on the 60th postoperative day ($P < 0.05$).

Table 4 shows the surgical complications and recurrence. We found 2.6% of hemorrhoidal thrombosis and 2.6% of anal skin tags. There was one "failure" case (2.6%) in a patient with a prior healing defect from a previous surgery. The low recurrence rate (2.6%) after 90 days demonstrates the efficacy of the treatment, even in cases of skin tags. All complications were classified as grade I using the Clavien-Dindo system. On day 60 post-op, there were no reports of fecal incontinence according to Wexner Scale.

Table 2. Sample Characteristics and Demographics

Characteristic	N = 38
Gender	
Female	13 (34.2%)
Male	25 (65.7%)
Age (y) (median, range)	49 (19–74)
Constipation	12 (31.5%)
Smoker	5 (13.1%)
Opioid use	8 (21.0%)
Localization of AF	
Anterior	3 (7.9%)
Posterior	35 (92.1%)
Skin tags before surgery	7 (26.9%)
Previous orificial surgery	10 (26.3%)
Hemorrhoidectomy	4 (10.5%)
Fissurectomy	3 (7.9%)
Rubber band ligation	1 (2.6%)
Bowel transit reconstruction	1 (2.6%)
Fistulotomy	1 (2.6%)
Time since diagnosis (median, range)	19 (1-144) months

Discussion

Anal fissures are difficult to treat; they present a challenge to colorectal surgeons. Although non-surgical methods usually successfully treat more than 90% of acute fissures, this rate decreases to 34% with chronic fissures that have persisted for more than six months.[22]

Efforts are focused on finding a medical treatment or non-invasive intervention that is as successful as surgical treatment for treating AFs and achieving fissure healing, muscle relaxation, and consequent pain relief. Numerous techniques have been proposed, including potent analgesics, nitrites, botulinum toxin, electrostimulation, and caudal epidural injections.[2,4,5,7,23-26]

The most important factor affecting the choice of treatment of AFs is whether the cleft is acute or chronic; nearly 60% of colorectal surgeons opt for topical nitrite or botulinum toxin in cases of both acute and chronic fissures.[27]

However, the efficacy of topical agents remains uncertain. A recent systematic review and meta-analysis of 37 studies highlighted low-certainty evidence that topical nitrates are an effective treatment for anal cleft healing and pain reduction compared with placebo options.[28] Despite the widespread use of topical diltiazem, more evidence is necessary to establish the efficacy of calcium channel blockers compared with placebos.[28]

Botulinum toxin has been described in several studies as a minimally invasive and safe treatment for the management of chronic AFs, particularly in patients at risk of incontinence. This treatment has several advantages over other methods.[29] However, some studies have documented progressive recurrence over time, with lower cure rates than what was initially reported.[30] These results may be related to the toxin's reversible effect and the disease's natural history. In a recent meta-analysis, botulinum toxin was not found to be superior compared with topical treatments.[30]

Neurostimulation techniques, such as posterior tibial nerve stimulation, have been shown to rapidly alleviate pain and facilitate fissure healing, particularly in the short to medium timeframe.[31] This non-invasive intervention is associated with a low risk of complications, rendering it an appealing choice for patients. However, research has indicated that the long-term efficacy of neurostimulation in improving the symptoms of AFs may not be as high as that of lateral internal sphincterotomy.[31]

Internal lateral sphincterotomy is an effective procedure and is still the gold standard surgery for chronic AFs that did not respond to conservative treatments. This procedure results in healing in more than 90% of patients.[9,10,13] However, internal lateral sphincterotomy

Table 3. Visual Analog Scale Scores Over Time

Measure	Time (days)	Average ± SD	Median(Q1–Q3)	Minimum	Maximum	*P* Value*
VAS	D0	4.1 ± 2.3	4 (2–6)	0	8	-
VAS	D7	2.3 ± 1.9	2 (0–4)	0	6	0.0118
VAS	D15	0.8 ± 1.2	0 (0–2)	0	4	< 0.0001
VAS	D30	0.3 ± 1.0	0 (0–0)	0	4	< 0.0001
VAS	D60	0.1 ± 0.7	0 (0–0)	0	4	< 0.0001

Abbreviations: VAS, visual analog scale; SD, standard deviation; Q1, first quartile; Q3, third quartile.
* Statistical significance $P < 0.05$

Table 4. Surgical Complications and Recurrence

Characteristic (N = 38)	No. (%)
Complication type	3 (7.9)
Hemorrhoidal Thrombosis	1 (2.6)
Skin tags	1 (2.6)
"Failure"	1 (2.6)
Complication classification[a]	
Grade I	3 (100)
Grade II	0 (0)
Grade III	0 (0)
Grade IV	0 (0)
Grade V	0 (0)
Recurrence	1 (2.6)
Incontinence after the procedure	0 (0)

[a] Complications according to the Clavien-Dindo system.[21]

is associated with an incontinence rate of approximately 4%.[23] A systematic review reported that internal lateral sphincterotomy is associated with the highest rate of healing and should be considered the primary treatment option after initial therapies with botulinum toxin or medical management prove to be unsuccessful.[28] Additionally, botulinum toxin exhibits comparable effectiveness to medical treatments.[28]

Continence-related problems are the most serious complications of lateral sphincterotomy.[28] More and more studies in recent years have focused on less-invasive methods which are less likely to result in incontinence. Lasers are being increasingly used in cases of benign anorectal conditions with good results.[14,16,31-36] Lasers show promising results and may represent a viable alternative for managing AFs.[14,34,36]

Using high-power lasers, such as laser diodes, in a non-focal manner or with lower power achieves the same modulatory effects as low-power lasers.[37] An in vitro study of the photobiomodulation achieved by the laser diodes in mesenchymal cells demonstrated a reduction in the inflammatory process and maintenance of cell viability through the positive effect of the laser on the production of IL-10 (anti-inflammatory) and VEGF (regulator of tissue angiogenesis).[37]

Unlike other laser surgeries (e.g., hemorrhoidectomy and pilonidal disease laser surgery), LFT is not associated with tissue ablation.[32,38] The responses to the use of light occurs via the respiratory cycle at the cellular level; cytochrome c oxidase present in the mitochondria as chromophores leads to increased synthesis of adenosine triphosphate (ATP), RNA, and proteins, increased oxygen consumption, boosted mitochondrial membrane potential, NADH and ATP synthesis, the production of oxygen free radicals, and the release of nitric oxide.[39,40] Nitric oxide is the primary inhibitory neurotransmitter that mediates the neurogenic relaxation of the anal sphincter and is one of the main mediators released by the tissue's response to light.[37,41]

Conventionally, the photobiological effects of laser radiation can be divided into short-term and long-term. Short-term responses are those in which the effect can be observed within a few seconds or minutes of irradiation. On the other hand, long-term effects occur within hours or even days after the conclusion of irradiation and typically involve new cell biosynthesis, especially during the proliferative phase of inflammation. [39]

The tissue repair process is complex and comprises vascular and cellular changes, epithelial and fibroblast proliferation, collagen synthesis and deposition, elastin and proteoglycan production, revascularization, and wound contraction.[42] Laser therapy produces trophic-regenerative, anti-inflammatory, and analgesic effects, in addition to generating an increase in mitochondrial activity and a consequent increase in ATP, vasodilation, protein synthesis, a decrease in prostaglandin levels, an increase in cell mitosis and migration, and the proliferation of keratinocytes and neoangiogenesis.[42]

Using high-power lasers has become a common practice for wound treatment in various medical specialties.[43,44] By combining different laser energies, it is possible to increase the depth of the photobiomodulation without promoting thermal injuries.[45] The literature has reported fluencies ranging from 4 J/cm^2 for class III lasers to 80 J/cm^2 for class IV lasers. [43]

Although our understanding of the mechanisms of action of photobiomodulation is far from complete, we have learned that antimicrobial efficacy does not appear to be affected by the resistance of the germs to antibiotics and does not select resistant germs after repeated applications. These findings are extremely valuable for contaminated areas, such as those with proctologic diseases. [46] However,

there have been few studies pertaining to the use of lasers for treating AFs. [14,17,33,34]

In 2015, Nasr Esfahani et al published a retrospective clinical study examining the use of the carbon dioxide laser fractional technique to treat 25 patients diagnosed with chronic AFs.[14] The procedure involved removing fibrotic and granulation tissues by laser beaming the base and edges of the fissure. The CO laser was used continuously (power: 15–18 W and 4 mm in depth). Significant improvements were observed in pain, bleeding, and constipation. None of the patients experienced recurrence, fecal incontinence, or an inability to control gas passage during the 1-year follow-up period.[14]

In 2016, Fateh et al studied 300 patients and compared the results of surgery with the use of a diode laser.[34] The team found that the average healing time and pain response were not significantly different between surgery (lateral intern sphincterotomy) and laser therapy in the first and third months. However, the two patient groups differed significantly in their pain response in the sixth month, and the laser-treated group remained asymptomatic. These findings suggest that while the short-term results are similar between surgery and laser therapy, the latter yields more satisfactory long-term results than cleft surgery, with fewer associated complications. Fateh et al. did not specify the power of their laser.[34]

In 2017, Pappas and Christodoulou published a review of 200 cases of laser electrocoagulation of AFs. All of the patients this team studied experienced immediate improvement and achieved healing within one month, with no recurrence and no cases of incontinence. The amount of energy was not described.[33]

Iacopo et al. treated 29 patients using a laser system that consisted of a CO_2 laser with a maximum power of 80 W and a second 50-W 980 nm diode laser source fiber delivery, which is helpful for procedures requiring higher coagulative power. Twenty-six out of the 29 patients had a mean pain intensity less than or equal to 3, which was considered a major endpoint. At the 1-month follow-up, the study's final success rate was 89.7%. After the follow-up period, there was a statistically significant reduction in pain and anal itching. There was also a drop in bleeding and burning maximum pain. Reepithelization was incredibly quick and successful: 22 out of 29 patients (i.e., 76%) exhibited full healing during a one-month follow-up; five patients exhibited partial reepithelization.[17]

Our study also showed good results regarding pain. There was a significant reduction in postoperative pain intensity over time (D0, D7, D15, D30, and D60) in patients undergoing LFT measured by the VAS. There was no fecal incontinence 60 days postoperatively, according to the Wexner Scale.

Since there was no excision of the fissure bed and no skin tags, 27% of the patients in our study retained residual skin tags after the procedure. Only one patient who had a post-hemorrhoidectomy healing defect (residual fissure) presented persistent symptoms and maintenance of the fissure. It is known that the pathophysiology of these cases may be affected by the surgical technique (e.g., maintenance of an exiguous cutaneous mucosal bridge).

In our study, 26% of the patients had post-operatory fissures. Many previous studies have excluded patients with earlier anal surgeries. Although sphincterotomy is the procedure of choice for chronic AFs in patients with no underlying incontinence, it is not considered first-line therapy in women with prior obstetrical or sphincter injuries and inflammatory bowel disease, or individuals who have undergone previous anorectal operations.[18] This fact may render laser therapy more attractive for patients with post-operatory fissures.

Although the passage of hard stool is one cause of AFs, our study showed that only 31% of the patients referred to chorionic constipation. This fact is consistent with the literature; a review showed that only 25% of patients with AFs had chronic constipation.[25]

The use of this proposed treatment modality is very promising. It offers rapid pain relief, a preponderant symptom in this pathology, and a minimal risk of fecal incontinence. Fecal incontinence is the most feared complication of the surgery currently considered the gold standard in the treatment of AFs.

Several studies have demonstrated increased healing using photobiomodulation. There is accordingly increasing interest in this treatment modality in proctologic pathologies that cause disabling pain, which is the case with AFs. Issues of embarrassment and difficulties finding available specialists can postpone the resolution of the condition, thereby causing harm to patients.[47,48]

Limitations of this study included its relatively small number of included patients. Furthermore, acute, chronic, and postoperative AFs were placed in the same group, and the physical characteristics of the AFs (e.g., the presence of sentinel skin tags and hypertrophic papillae) were not described in detail. This study focused mostly on pain symptoms, and other factors were not studied in detail. While the available evidence suggests that laser-based treatments may be a viable alternative for treating AFs, additional research is necessary to establish the long-term efficacy and safety profile of this technique more fully. Larger, randomized controlled trials are necessary to compare laser therapies with established surgical and pharmacological interventions and optimize treatment parameters.

Conclusion

These results suggest that the treatment of AFs with laser therapy results in a significant reduction in the intensity of postoperative pain, both immediately and over time. Furthermore, there were no changes in fecal continence

at the end of the follow-up period. Additional studies that better categorize AFs and include more cases and longer follow-up times are necessary.

Acknowledgments
The authors thank all the Laser Academy members for their cooperation.

Authors' Contribution
Conceptualization: Abel Botelho Quaresma.
Data curation: Luana Perondi, Abel Botelho Quaresma, Elisa Treptow Marques, Marcelo Marciano, Rodnei Bertazzo Sampietro.
Formal analysis: Fabrício Doin Paz de Oliveira, Ana Carolina Buffara Blitzkow.
Funding acquisition: Fabrício Doin Paz de Oliveira.
Investigation: Ana Carolina Buffara Blitzkow, Sônia Cristina Cordeiro Time, Elisa Treptow Marques.
Methodology: Abel Botelho Quaresma, Ana Carolina Buffara Blitzkow, Sônia Cristina Cordeiro Time, Fabrício Doin Paz de Oliveira.
Project administration: Ana Carolina Buffara Blitzkow.
Resources: Fabrício Doin Paz de Oliveira.
Software: Ana Carolina Buffara Blitzkow, Fabrício Doin Paz de Oliveira.
Supervision: Ana Carolina Buffara Blitzkow.
Validation: Abel Botelho Quaresma.
Visualization: Ana Carolina Buffara Blitzkow, Elisa Treptow Marques, Sônia Cristina Cordeiro Time.
Writing–original draft: Abel Botelho Quaresma, Luana Perondi, Ana Carolina Buffara Blitzkow, Sônia Cristina Cordeiro Time.
Writing–review editing: Ana Carolina Buffara Blitzkow, Sônia Cristina Cordeiro Time, Fabrício Doin Paz de Oliveira, Elisa Treptow Marques, Abel Botelho Quaresma.

Competing Interests
The authors declare that they have no conflict of interests.

Ethical Approval
This study was approved by UNOESTE University (Ethical approval No.: "Plataforma Brasil" 63897722.9.0000.5367).

Funding
None.

References
1. Newman M, Collie M. Anal fissure: diagnosis, management, and referral in primary care. Br J Gen Pract. 2019;69(685):409-10. doi: 10.3399/bjgp19X704957.
2. Ebinger SM, Hardt J, Warschkow R, Schmied BM, Herold A, Post S, et al. Operative and medical treatment of chronic anal fissures-a review and network meta-analysis of randomized controlled trials. J Gastroenterol. 2017;52(6):663-76. doi: 10.1007/s00535-017-1335-0.
3. Mapel DW, Schum M, Von Worley A. The epidemiology and treatment of anal fissures in a population-based cohort. BMC Gastroenterol. 2014;14:129. doi: 10.1186/1471-230x-14-129.
4. Beaty JS, Shashidharan M. Anal Fissure. Clin Colon Rectal Surg. 2016;29(1):30-7. doi: 10.1055/s-0035-1570390.
5. Ahmad Salati S. Anal Fissure - an extensive update. Pol Przegl Chir. 2021;93(4):46-56. doi: 10.5604/01.3001.0014.7879.
6. Shahid MH, Javed S, Javed S, Khan AZ, Kaiser A, Mithany RH. Comparative efficacy of topical metronidazole and glyceryl trinitrate versus topical glyceryl trinitrate alone in the treatment of acute anal fissure: a randomized clinical trial. Cureus. 2022;14(11):e31812. doi: 10.7759/cureus.31812.
7. Tutino R, Nigro C, Paternostro F, Federico R, Lo Secco G, Gallo G, et al. Fissurectomy versus lateral internal sphincterotomy in the treatment of chronic anal fissures: no advantages in terms of post-operative incontinence. Tech Coloproctol. 2023;27(10):885-9. doi: 10.1007/s10151-023-02780-8.
8. Asefa Z, Awedew AF. Comparing closed versus open lateral internal sphincterotomy for management of chronic anal fissure: systematic review and meta-analysis of randomised control trials. Sci Rep. 2023;13(1):20957. doi: 10.1038/s41598-023-48286-z.
9. Bara BK, Mohanty SK, Behera SN, Sahoo AK, Swain SK. Fissurectomy versus lateral internal sphincterotomy in the treatment of chronic anal fissure: a randomized control trial. Cureus. 2021;13(9):e18363. doi: 10.7759/cureus.18363.
10. Liang J, Church JM. Lateral internal sphincterotomy for surgically recurrent chronic anal fissure. Am J Surg. 2015;210(4):715-9. doi: 10.1016/j.amjsurg.2015.05.005.
11. Hancke E, Suchan K, Voelke K. Anocutaneous advancement flap provides a quicker cure than fissurectomy in surgical treatment for chronic anal fissure-a retrospective, observational study. Langenbecks Arch Surg. 2021;406(8):2861-7. doi: 10.1007/s00423-021-02227-4.
12. Sobrado Júnior CW, Hora JA, Sobrado LF, Guzela VR, Nahas SC, Cecconello I. Anoplasty with skin tag flap for the treatment of chronic anal fissure. Rev Col Bras Cir. 2019;46(3):e20192181. doi: 10.1590/0100-6991e-20192181.
13. Abramowitz L, Bouchard D, Souffran M, Devulder F, Ganansia R, Castinel A, et al. Sphincter-sparing anal-fissure surgery: a 1-year prospective, observational, multicentre study of fissurectomy with anoplasty. Colorectal Dis. 2013;15(3):359-67. doi: 10.1111/j.1463-1318.2012.03176.x.
14. Nasr Esfahani M, Madani G, Madhkhan S. A novel method of anal fissure laser surgery: a pilot study. Lasers Med Sci. 2015;30(6):1711-7. doi: 10.1007/s10103-015-1771-0.
15. Trigui A, Rejab H, Akrout A, et al. Laser utility in the treatment of hemorrhoidal pathology: a review of literature. Lasers Med Sci. 2022;37(2):693-699. doi:10.1007/s10103-021-03333-x.
16. Elfallal AH, Fathy M, Elbaz SA, Emile SH. Comprehensive literature review of the applications of surgical laser in benign anal conditions. Lasers Med Sci. 2022;37(7):2775-89. doi: 10.1007/s10103-022-03577-1.
17. Iacopo G, Tommaso C, Chiara L, Filippo C, Paolo D, Gianni R, et al. Scanner-assisted CO2 laser fissurectomy: a pilot study. Front Surg. 2021;8:799607. doi: 10.3389/fsurg.2021.799607.
18. Davids JS, Hawkins AT, Bhama AR, Feinberg AE, Grieco MJ, Lightner AL, et al. The American society of colon and rectal surgeons clinical practice guidelines for the management of anal fissures. Dis Colon Rectum. 2023;66(2):190-9. doi: 10.1097/dcr.0000000000002664.
19. Breivik H, Borchgrevink PC, Allen SM, Rosseland LA, Romundstad L, Hals EK, et al. Assessment of pain. Br J Anaesth. 2008;101(1):17-24. doi: 10.1093/bja/aen103.
20. Jorge JM, Wexner SD. Etiology and management of fecal incontinence. Dis Colon Rectum. 1993;36(1):77-97. doi: 10.1007/bf02050307.
21. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg. 2004;240(2):205-13. doi: 10.1097/01.sla.0000133083.54934.ae.
22. Emile SH, Elgendy H, Elfeki H, Magdy A, Abdelmawla AA, Abdelnaby M, et al. Does the duration of symptoms of anal fissure impact its response to conservative treatment? A prospective cohort study. Int J Surg. 2017;44:64-70. doi: 10.1016/j.ijsu.2017.06.044.

23. Nelson RL, Manuel D, Gumienny C, Spencer B, Patel K, Schmitt K, et al. A systematic review and meta-analysis of the treatment of anal fissure. Tech Coloproctol. 2017;21(8):605-25. doi: 10.1007/s10151-017-1664-2.
24. Stewart DB Sr, Gaertner W, Glasgow S, Migaly J, Feingold D, Steele SR. Clinical practice guideline for the management of anal fissures. Dis Colon Rectum. 2017;60(1):7-14. doi: 10.1097/dcr.0000000000000735.
25. Collins EE, Lund JN. A review of chronic anal fissure management. Tech Coloproctol. 2007;11(3):209-23. doi: 10.1007/s10151-007-0355-9.
26. Gökçek E, Gökçe R, Kaçar CK. The effect of caudal epidural injection on healing in the treatment of chronic anal fissure. Medicine (Baltimore). 2023;102(37):e35160. doi: 10.1097/md.0000000000035160.
27. Balla A, Saraceno F, Shalaby M, Gallo G, Di Saverio S, De Nardi P, et al. Surgeons' practice and preferences for the anal fissure treatment: results from an international survey. Updates Surg. 2023;75(8):2279-90. doi: 10.1007/s13304-023-01661-x.
28. Jin JZ, Bhat S, Park B, Hardy MO, Unasa H, Mauiliu-Wallis M, et al. A systematic review and network meta-analysis comparing treatments for anal fissure. Surgery. 2022;172(1):41-52. doi: 10.1016/j.surg.2021.11.030.
29. Bobkiewicz A, Francuzik W, Krokowicz L, Studniarek A, Ledwosiński W, Paszkowski J, et al. Botulinum toxin injection for treatment of chronic anal fissure: is there any dose-dependent efficiency? A meta-analysis. World J Surg. 2016;40(12):3064-72. doi: 10.1007/s00268-016-3693-9.
30. Sierra-Arango F, de la Hoz-Valle J, Espinosa JP, Moreno-Montoya J, Vásquez Roldan M, Pérez-Riveros ED. Clinical outcomes of medical management options for chronic anal fissures in a long-term follow-up: systematic review and meta-analysis. Dig Dis. 2023;41(5):822-32. doi: 10.1159/000528222.
31. Bananzadeh A, Sohooli M, Shamsi T, Darabi M, Shahriarirad R, Shekouhi R. Effects of neuromodulation on treatment of recurrent anal fissure: a systematic review. Int J Surg. 2022;102:106661. doi: 10.1016/j.ijsu.2022.106661.
32. Paz Oliveira FD, Time SC, Blitzkow AC, Boarini LR, Munhóz AA, Mont'Alverne RE. Minimum energy laser pilonidotomy (MELPi): a multicenter study of a novel method in pilonidal disease. Updates Surg. 2024;76(3):1025-30. doi: 10.1007/s13304-024-01848-w.
33. Pappas AF, Christodoulou DK. A novel minimally invasive treatment for anal fissure. Ann Gastroenterol. 2017;30(5):583. doi: 10.20524/aog.2017.0173.
34. Fateh SH, Darvish-Shafighi S, Norouzi A, Kalantari M. Outcome of laser therapy in patients with anal fissure. Hamdan Med J. 2016;9(1):69-73. doi: 10.7707/hmj.423.
35. Solari S, Martellucci J, Annicchiarico A, Scheiterle M, Bergamini C, Prosperi P. Laser technology in proctological diseases: is it really the wave of the future? Updates Surg. 2023;75(7):1759-72. doi: 10.1007/s13304-023-01578-5.
36. Ambe PC. Laser interventions in coloproctology. A plea for standardized treatment protocols. Tech Coloproctol. 2023;27(10):953-5. doi: 10.1007/s10151-023-02859-2.
37. Havel M, Betz CS, Leunig A, Sroka R. Diode laser-induced tissue effects: in vitro tissue model study and in vivo evaluation of wound healing following non-contact application. Lasers Surg Med. 2014;46(6):449-55. doi: 10.1002/lsm.22256.
38. Lie H, Caesarini EF, Purnama AA, Irawan A, Sudirman T, Jeo WS, et al. Laser hemorrhoidoplasty for hemorrhoidal disease: a systematic review and meta-analysis. Lasers Med Sci. 2022;37(9):3621-30. doi: 10.1007/s10103-022-03643-8.
39. Neri L. Estudo histológico dos efeitos da lesão com laser diodo 980 nm e 1470 nm em pregas vocais de coelhos [dissertation]. Universidade de São Paulo; 2019. doi: 10.11606/T.5.2019.TDE-16042019-115121.
40. Huang YY, Sharma SK, Carroll J, Hamblin MR. Biphasic dose response in low level light therapy - an update. Dose Response. 2011;9(4):602-18. doi: 10.2203/dose-response.11-009.Hamblin.
41. Simunovic Z. Low level laser therapy with trigger points technique: a clinical study on 243 patients. J Clin Laser Med Surg. 1996;14(4):163-7. doi: 10.1089/clm.1996.14.163.
42. Khalkhal E, Razzaghi M, Rostami-Nejad M, Rezaei-Tavirani M, Heidari Beigvand H, Rezaei Tavirani M. Evaluation of laser effects on the human body after laser therapy. J Lasers Med Sci. 2020;11(1):91-7. doi: 10.15171/jlms.2020.15.
43. Lu Q, Yin Z, Shen X, Li J, Su P, Feng M, et al. Clinical effects of high-intensity laser therapy on patients with chronic refractory wounds: a randomised controlled trial. BMJ Open. 2021;11(7):e045866. doi: 10.1136/bmjopen-2020-045866.
44. Pereira FL, Ferreira MV, da Silva Mendes P, Rossi FM, Alves MP, Alves BL. Use of a high-power laser for wound healing: a case report. J Lasers Med Sci. 2020;11(1):112-4. doi: 10.15171/jlms.2020.19.
45. Abdul Munap DH, Suan Lau P, Bidin N, Bakhtiar H, Krishnan G. Effects of photobiomodulation therapy with various laser power densities on wound healing. J Phys Conf Ser. 2019;1151(1):012011. doi: 10.1088/1742-6596/1151/1/012011.
46. Hamblin MR, Abrahamse H. Can light-based approaches overcome antimicrobial resistance? Drug Dev Res. 2019;80(1):48-67. doi: 10.1002/ddr.21453.
47. Mosca RC, Ong AA, Albasha O, Bass K, Arany P. Photobiomodulation therapy for wound care: a potent, noninvasive, photoceutical approach. Adv Skin Wound Care. 2019;32(4):157-67. doi: 10.1097/01.ASW.0000553600.97572.d2.
48. Rashidi S, Yadollahpour A, Jalilifar M, Naraqi Arani M, Rezaee Z. Laser therapy for wound healing: a review of current techniques and mechanisms of action. Biosci Biotechnol Res Asia. 2015;12:217-3. doi: 10.13005/bbra/1626.