Original Article

Comparative Efficacy of Medical Treatment Versus Surgical Sphincterotomy in the Treatment of Chronic Anal Fissure

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Abstract

Background: Anal fissure which is defined as a longitudinal tear in anoderm below the dentate line is one of the most common benign diseases of anorectal area. Severe pain during the defecation and emotional stress that it causes may reduce people's quality of life. **Aims:** In this randomized clinical trial, we aimed to compare the efficiency of the topical ointment with medical treatment and surgical lateral internal sphincterotomy. **Method:** This is a randomized clinical trial of 550 patients who were treated for chronic anal fissure. Patients were randomly divided into 4 groups according to the treatment type they received. **Results:** In a vast majority of the patients, the primary complaint was pain (92.3%) and bleeding during defecation (62%). Both pain relief and healing of the fissure, which are the components of response to treatment, had not been observed in 56 (37.3%) patients of topical nitroglycerin ointment group until the second month. Among the recalcitrant patients in both topical nitroglycerin (56) and topical diltiazem ointment (47) groups, 27 (48.2%), and 36 (76.5%) patients underwent surgery, respectively. The best response to treatment was also obtained in lateral internal sphincterotomy group. **Conclusion:** LIS is still the gold standard for the treatment of chronic anal fissure when the physicians would like to avoid recurrence and obtain the best pain relief.

Keywords: *Chronic anal fissure, LIS, medical, partial, treatment*

Background

Anal fissure is a longitudinal tear in anoderm below the dentate line, which is mostly located posteriorly in the midline.[1] It is one of the most common benign diseases of anorectal area, and due to the severe pain during the defecation and emotional stress that it causes, it may also lower people's quality of life.[2] The etiology is still unclear. However, it is considered to be associated with the significant increase in sphincter pressure (even at rest) with the passage of hard stool.[3]

Acute anal fissures often heal within 1-2 weeks, while the healing of the chronic anal fissures takes longer than 8-12 weeks and in addition a hypertrophic papilla and a sentinel tubercle accompany the chronic anal fissure and the sphincter muscle fibers at the base of the tear are exposed.[4,5]

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Basically, treatment for anal fissure usually comprises reducing the sphincter pressure with physical or chemical methods. Studies on the methods of treatment of chronic anal fissures range from medical applications to surgery. There is no general agreement on ideal therapy for chronic anal fissures.[6]

The American Society of Colon and Rectal Surgeons (ASCRS) recommends conservative treatment as the initial treatment choice which includes stool softeners, high fiber diet and warm sitz bath.[7] However, a significant number of patients do not respond this conservative treatment. Further treatment options

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will therefore be required. In this case, next step is combination of conservative management and medical treatment. The most important disadvantage of medical treatment is high recurrence rate. Lateral internal sphincterotomy (LIS) is considered to be the gold standard surgical management of chronic anal fissures when conservative and medical treatment fails.[8] Although LIS is an effective procedure, it has its own risks. The incidence of incontinence after LIS is reported as 0-47%.[9]

In this a randomized clinical trial, we aimed to compare the efficacy of the topical ointment with diltiazem and/or nitroglycerin treatment (medical treatment) and surgical lateral internal sphincterotomy.

Method

The study protocol was approved by the institutional Ethics Committee approved date: 01/12/2010, number: 31829978-050.01.04-E.1700085966. A written informed consent forms were obtained from the patients when they were first diagnosed with anal fissure. Patients were informed about the treatment and the study in detail, along with which further treatment options and probable complications were explained. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Study design

The study protocol was approved by the institutional Ethics Committee. This study is a randomized clinical study in which 550 patients who were treated for chronic anal fissure in our General Surgery Department between January 2010 and October 2017 were included.

The candidates for medical treatment were evaluated in outpatients clinics and decision of which medical agent to use was determined by the clinicians who did not know that the patient was included in the study according to her/his personal preference. Same randomization protocol was followed for the type of surgery. Inclusion criteria were suffering from anal fissure for more than 6 weeks, exposed fibers of internal sphincter, appearance of sentinel tubercle and hypertrophied anal papilla for supporting the diagnosis of chronic fissure. Patients with simultaneous anal abscesses, anal fistula and/or hemorrhoidal diseases, diagnosis of inflammatory bowel diseases (IBD), lactating women, patients with limited cooperation and patients who left or did not regularly apply medical treatment were excluded from the study. The patients had no history of anal or rectal cancer.

Patients were asked to fill out a questionnaire that queried their symptoms. Anal pain was assessed before beginning treatment and at follow-up visits using a linear visual analog pain score. Anal incontinence was assessed by means of a validated scoring and grading system, as previously reported by Pescatori *et al*.[10]

Patients and grouping

Patients were randomly divided into the following 4 groups:

Group A: Treated with topical nitroglycerin ointment (150 patients)
Group B: Treated with topical diltiazem ointment (150 patients)
Group C: Performed lateral internal sphincterotomy (200 patients)
Group D: Performed partial lateral internal sphincterotomy (50 patients)

Medical treatment

8 weeks of topical ointment application (0.2% nitroglycerin or 2% diltiazem applied every 12 hours) followed by warm sitz bath constituted the medical treatment.

Surgical procedures

Both surgical procedures (LIS and Partial LIS) were carried out in the lithotomy position with open sphincterotomy under general or regional anesthesia. The anal canal was visualized with an anoscope, a longitudinal incision was made in the anoderm, and the distal half of the internal anal sphincter was divided under direct vision followed by closure of the mucosa. Internal anal sphincter was almost completely cut in LIS, while 50-80% part of the muscle was cut in the partial procedure. Procedures were performed by six different surgeons experienced in benign anorectal disorders.

Postoperative management and follow-up

Prophylactic cephazolin or gentamicin when patient is allergic to penicillin and metronidazole were administered intravenously 30 minutes before skin incision to all patients. A single dose of a non-steroidal anti-inflammatory drug (NSAID) was injected intramuscularly on recovery and was repeated if additional analgesia was needed. Oral metronidazole twice daily for one week was given postoperatively. NSAID and stool softeners were also prescribed to be used when needed at hospital discharge.

Follow-up was scheduled as first, second, fourth and eighth weeks of post-operative period. Anorectal examination was performed during every follow-up clinic visit and fissure healing was monitored. Pain relief was also assessed by using a visual analog scale which represented a severity of pain from 0 (no pain) to 10 (worst imaginable pain).

The medical records of the patients were reviewed and demographic data (sex, age), medical history, presenting

symptoms and findings, first-second-fourth-eighth week examination findings, response to the treatment (pain relief and evaluation of the fissure, erythema and/or inflammation), side effects of the treatment and presence of recurrence of the disease were recorded and analyzed.

Statistical analysis

To compare the differences between three and more groups, one-way analysis of variance was used when the parametric test prerequisites were fulfilled, and the Kruskal Wallis test was used when such prerequisites were not fulfilled. The Bonferroni correction method, which is a multiple comparison test, was used to evaluate the significant results concerning 3 and more groups.

Chi-square test was used for determining the relationships between two discrete variables. When the expected sources were less than 20%, values were determined through the Monte Carlo Simulation Method in order to include such sources in analysis.

The data were evaluated via SPPS 20 (IBM Corp. Released 2011. IBM SPSS Statistics for Windows, Version 20.0. Armonk, NY: IBM Corp.). P <0.001 were taken as significance levels.

Results

In a period of 7 years (2010-2017), 550 patients (310 male) were followed in 4 different groups. Demographics of the patients are given in Table 1.

There is no statistically significant difference between groups in terms of gender and age distribution. It appears that 440 (80%) of the fissures were located posteriorly and 110 (20%) were anterior. In vast majority of the patients, the primary complaint was pain (92.3%) and bleeding during defecation (62%). Additionally the other major complaints were constipation, pruritus and perianal discharge. There is no statistical difference between the groups in terms of pain, pruritus and perianal discharge. Bleeding and constipation had higher frequency in the groups which underwent surgical treatment.

The patients had been evaluated at first, second, fourth and eighth weeks from the beginning of the treatment for assessing the response to treatment and the status of complaints [Table 2].

Pain relief was not observed in 39 and 48 patients at the end of the eighth week in group A and B, respectively. At the end of the 8th week, 18 patients from group C and 8 patients from group D still had pain. Best pain relief was observed in group C. From the patients who still had pain in group C, 2 were found to have pain due to newly developed thrombosed hemorrhoids, while 2 had perianal abscess. These patients relieved after thrombectomy and drainage of the perianal abscess.

Results of the recovery of fissure are shown in Table 3.

Both pain relief and healing of the fissure which were previously attributed as the components of the response to treatment were not observed in 56 patients from group A until the second month. There was no response to treatment in 47 patients from group B. As a result of that, 27 of those 56 patients from group A, and 36 of these 47 patients from group B underwent surgery.

Fourteen patients from group C and seven patients from group D did not have any relief from their fissure. When

Table 1: Clinical profile of study groups

	Group A (*n*:150)	Group B (*n*:150)	Group C (*n*:200)	Group D (*n*:50)	*P*
Clinical features					
Male (%)	84 (56%)	82 (54.7%)	116 (58%)	28 (56%)	0.852
Female (%)	66 (44%)	68 (45.3%)	84 (42%)	22 (44%)	
Age (years); mean	38.21±9.74	37.84±10.49	37.95±10.82	35.68±9.64	0.754
Complaints					
Pain (%)	140 (93.3%)	135 (90%)	189 (94.5%)	44 (88%)	0.752
Bleeding (%)	70 (46.7%)	85 (56.7%)	156 (78%)	34 (68%)	<0.001*
Constipation (%)	25 (16.7%)	30 (20%)	74 (37%)	18 (36%)	<0.001*
Itching (%)	15 (10%)	18 (12%)	34 (17%)	12 (24%)	0.523
Perianal discharge (%)	5 (3.3%)	4 (2.7%)	7 (3.5%)	1 (2%)	0.436

Table 2: Results of pain relief

Number of patients whose complaints relieved	Group A (*n*:150)	Group B (*n*:150)	Group C (*n*:200)	Group D (*n*:50)	*P*
First week (%)	74 (49.3%)	68 (45.3%)	126 (63%)	26 (52%)	<0.001*
Second week (%)	96 (64%)	81 (54%)	154 (77%)	35 (70%)	<0.001*
Fourth week (%)	102 (68%)	88 (58.7%)	174 (87%)	38 (76%)	<0.001*
Eighth week (%)	111 (74%)	102 (68%)	182 (91%)	42 (84%)	<0.001*

Table 3: Results of recovery of fissure

Number of patients recovered	Group A (*n*:150)	Group B (*n*:150)	Group C (*n*:200)	Group D (*n*:50)	*P*
First week (%)	0 (0%)	0 (0%)	76 (38%)	12 (24%)	<0.001*
Second week (%)	0 (0%)	2 (1.3%)	132 (66%)	26 (52%)	<0.001*
Fourth week (%)	11 (7.3%)	14 (9.3%)	164 (82%)	36 (72%)	<0.001*
Eighth week (%)	94 (62.7%)	103 (68.7%)	186 (93%)	43 (86%)	<0.001*

Table 4: Side effects and complications

Side effects and complications	Group A (*n*:150)	Group B (*n*:150)	Group C (*n*:200)	Group D (*n*:50)
Headache	22 (5.3%)			
Nausea		3 (1.3%)		
Arrhythmia		2 (1.3%)		
Gas incontinence (Transient)			2 (1%)	1 (2%)
Fluid incontinence			2 (1%)	
Perianal abscess			2 (1%)	

the groups were compared, it was found out that the best response to treatment was obtained in group C. In group D, the rate of recovery was higher than that of the groups (A and B) which had received medical treatment, yet it was statistically lower than group C's.

Side effects and complications

During the treatment period, there was intermittent headache in 22 patients from Group A and six of them were severe [Table 4]. Three patients had nausea and two patients developed arrhythmia in Group B.

Of the 14 patients who did not recover in group C, 8 had recurrence, 4 had incontinence (gas incontinence in 2, fluid incontinence in two2 and 2 had perianal abscess. 6 and one of the patients with recurrence were found to have one and two previous surgeries, respectively. The complaints of the patients with gas incontinence improved in the 4th post-operative month while the fluid incontinence of the other two patients was determined as persistent.

Of the patients who did not have any evidence of recovery in group D, recurrence was observed in six and gas incontinence was detected in one during the early period. 4 of the patients who had developed recurrence were re-operated, while the complaint of the patient who had incontinence passed after 6 months from the surgery.

During the first week, about 18% of the patients who underwent surgery had complaint of burning sensation in the anal region and only 4 (1.6%) of them stated that their complaint did not pass at the end of the eighth week.

Discussion

The aim of our study was to determine whether the categorization and outcomes of patients treated with LIS, partial LIS and medical treatment for anal fissure were comparable or not.

Anal fissure is a common and painful disease of the anal canal. The etiology of this disease still remains unclear. However it is considered to be derived from the hypertrophy of the internal sphincter and increased anal sphincter resting pressure resulting to ischemia of the anoderm.[11]

Management and optimal treatment of the disease are controversial. Many studies recommend conservative (such as habit regularization) and medical treatment modalities as the initial treatment options since they are non-invasive and do not have risks such as anal sphincter injury.[12-14] Commonly used medical substances are calcium channel blockers (diltiazem) and glyceryl trinitrate (nitric oxide derivatives) and alternative treatment methods (botulinum toxin injections, anal dilatation etc.) are also used.[5,15-17] With these treatments, the aim is to decrease the sphincter tone, obtain pain relief and improve the fissure.

However, in most cases, since the conservative and medical treatments provide temporary relief and have high recurrence rates, surgical sphincterotomy is still considered the gold standard.[18,19]

A prospective study by Valizedah *et al*. showed that, when compared to the patients who underwent LIS, the patients whom Botox injection (BI) was performed were found to have significantly higher recurrence rates (12% versus 76%) at the end of the 6 months of follow-up.[20] Another disadvantage of BI is its high cost. For this reason, it is indicated as an alternative method that can be preferred before surgery when medical treatment fails.[21]

Sphincterotomy was first proposed by Boyer in 1818.[22] Subsequently, surgical techniques such as fissurectomy, anal dilation, posterior/lateral sphincterotomy and advanced flap were discovered and applied.

The main goal of sphincterotomy is to increase the blood flow of the anoderm by decreasing the maximum anal sphincter pressure by 18-50%. This technique provides an improvement between 82% and 100% of cases.[11,23] These results are consistent with the findings of the previous studies.[24,25] Furthermore, there are publications in the literature reporting that partial sphincterotomy is also effective in reducing the risk of incontinence.[26] To the best of our knowledge, although there are many studies in the literature comparing medical treatment outcomes or the results of medical treatments and LIS, there is no comparative study that partial sphincterotomy was included and its efficacy is compared to other methods.

Our stage-based analysis revealed that even though the results of fissure healing in patients who underwent partial sphincterotomy were more promising than the ones who had medical treatment, its recurrence rate was higher than standard LIS. Moreover, the absence of permanent incontinence in any patient with partial LIS provides a great advantage.

Furthermore, we compared the duration until the pain relief had been achieved in each group according to their treatment types.

It was observed that the most effective pain palliation in early and late periods of the treatment was gained with LIS. These results were similar to those of previous studies.[27,28] On the other hand, according to our study, since the results of medical treatment for pain response was also satisfactory at the end of the eighth week (A = 74%, B = 68%), medical treatment can be preferred as a primary step in patients who declined consent for surgery.

In addition to their high rates of recurrence and temporary relief they provided, the side effects such as headache, anal rash, vomiting, tachycardia which occurred in 20-30% of patients are the limitations of the medical treatment modalities.[7,29]

According to our study, the side effects of the medical treatment modalities were similar to other studies. 22 patients using nitroglycerin ointment developed headache and, 3 and 2 patients using diltiazem ointment developed nausea and arrhythmia, respectively. However, none of the side effects was severe enough to interrupt the treatment.

Although LIS ensures the best results with the success rate above 90%, it still has a risk of fecal incontinence that cannot be ignored.[14] In varying severity, up to 47.6% of the patients developed post-operative disturbance of continence after LIS.[9,30] A novel meta-analysis showed that long-term risk of incontinence after LIS is significant (approximately 15%) with the obvious fecal incontinence rate of 1%.[9] Gas and/or liquid incontinence were seen in 2% of group C (four patients) and two patients with gas incontinence resolved without any intervention after four months, according to our data. However, other two patients had permanent incontinence.

Complications such as infection, abscess, fistula and hematoma may rarely occur after LIS.[31] Two of our patients were found to develop perianal abscess postoperatively and their complaints resolved with simple drainage.

Despite the high success rate in fissure healing after sphincterotomy, recurrence may occur between 1.6 and 6%.[19,32] The most common cause of recurrence is inadequate sphincterotomy. In such cases, sphincterotomy can be repeated.

Also, in our study, while the recurrence rate of LIS group was compatible with the literature, the rate was higher in the partial sphincterotomy group when compared to other studies (4% and 12%, respectively).

There exists a drawback in this study in that the number of the patients in partial LIS group is few. Further multicenter data analysis should be carried out in the future to test our results partial LIS. Besides, anal canal pressures are unknown since the anal manometer was not performed.

Conclusion

The results of this study support LIS as the gold standard treatment for chronic anal fissure when the clinicians would like to avoid recurrence and obtain the best pain relief. Since the most feared complication of the surgery is persistent incontinence, partial LIS can be considered as an effective surgical alternative. However, this inference should be strengthened with further studies. On the alternative, although several side effects may develop, medical treatment may be advanced as a primary step and applied safely with caution in patients who declined consent for surgery and/or not suitable for surgery.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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