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Can topical applicatıons be an alternative to surgery in the treatment of chronic anal fissures?

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Abstract

Introduction: Anal fissure, characterized by a painful ulcer in the anal canal, presents a significant medical challenge. While surgical approaches like lateral internal sphincterotomy (LIS) have been the gold standard for chronic anal fissures, they come with potential complications such as incontinence and abscess formation. In contrast, medical treatments, including topical glyceryl trinitrate and diltiazem, have emerged as alternatives, offering non-invasive options with potentially fewer complications.

Method: In this retrospective study, we evaluated 136 patients treated for chronic anal fissures between June 2019 and December 2022 at Balikesir University Hospital, comparing surgical and medical interventions. The study encompassed demographic analysis, treatment modalities, complete recovery, recurrence rates, and side effects/complications. Statistical analyses, including logistic regression, were performed to assess the efficacy and risks associated with different treatments.

Results: Our findings indicated a higher rate of complete recovery with surgical treatment (86.1%) compared to medical treatments (glyceryl trinitrate: 64.8%, diltiazem: 69.6%). However, no significant difference was observed in recurrence rates between treatment groups. Surgical intervention exhibited a higher incidence of complications such as incontinence and abscess formation, while medical treatments were associated with side effects like headache and gastrointestinal disturbances. Notably, diltiazem therapy showed outcomes comparable to other modalities, indicating its potential as an effective and safer alternative.

Conclusion: Despite the favorable outcomes of surgical treatment, considerations of potential complications underscore the importance of tailored approaches. Prospective, randomized controlled trials with larger cohorts are warranted to further elucidate the efficacy and safety profiles of medical treatments in chronic anal fissures, facilitating informed decision-making in clinical practice.

Key words: Lateral internal sphincterotomy, Fissure in ano, Nitroglycerin, Diltiazem

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Kronik anal fissür tedavisinde topikal uygulamalar cerrahiye bir alternatif olabilir mi?

Öz

Giriş: Anal fissür, anüs kanalında ağrılı bir ülserle karakterize edilen önemli bir tıbbi sorunu temsil etmektedir. Lateral internal sfinkterotomi (LIS) gibi cerrahi yaklaşımlar, kronik anal fissürler için altın standart olmuş olsa da, gaz veya dışkı kaçırma gibi potansiyel komplikasyonlarla ilişkilidir. Buna karşın, topikal gliseril trinitrat ve diltiazem gibi tıbbi tedaviler, daha az invaziv seçenekler sunarak potansiyel olarak daha az komplikasyona sahip alternatifler olarak ortaya çıkmıştır.

Yöntemler: Bu retrospektif çalışmada, Haziran 2019 ile Aralık 2022 tarihleri arasında Balıkesir Üniversitesi Hastanesi'nde kronik anal fissür tedavisi gören 136 hasta değerlendirilmiş, cerrahi ve tıbbi müdahaleler karşılaştırılmıştır. Çalışma demografik analiz, tedavi yöntemleri, tam iyileşme, nüks oranları ve yan etkiler/komplikasyonları içermiştir. Lojistik regresyon da dahil olmak üzere istatistiksel analizler, farklı tedavilerin etkililiğini ve ilişkili riskleri değerlendirmek için yapılmıştır.

Bulgular: Bulgularımız, cerrahi tedavi ile (%86,1) tıbbi tedaviler (gliseril trinitrat: %64,8, diltiazem: %69,6) karşılaştırıldığında, tam iyileşme oranının daha yüksek olduğunu göstermiştir. Ancak, tedavi grupları arasında nüks oranlarında anlamlı farklılık gözlenmemiştir. Cerrahi müdahalenin gaz veya dışkı kaçırma gibi komplikasyonların daha yüksek bir insidansı ile ilişkili olduğu, tıbbi tedavilerin ise baş ağrısı ve gastrointestinal rahatsızlıklar gibi yan etkilerle ilişkilendirildiği belirlenmiştir. Özellikle diltiazem tedavisi, diğer modalitelerle karşılaştırılabilir sonuçlar göstermiş ve etkili ve daha güvenli bir alternatif olarak potansiyelini ortaya koymuştur.

Sonuç: Cerrahi tedavinin olumlu sonuçlarına rağmen, potansiyel komplikasyonların değerlendirilmesi, kişiselleştirilmiş yaklaşımların önemini vurgulamaktadır. Kronik anal fissürlerde tıbbi tedavilerin etkililiği ve güvenlik profillerinin daha iyi anlaşılmasını sağlamak için daha geniş çaplı prospektif, randomize kontrollü çalışmaların yapılması gerekmektedir, bu da klinik uygulamada bilinçli karar verme sürecini kolaylaştıracaktır.

Anahtar kelimeler: Lateral internal sfinkterotomi, Anal fissür, Nitrogliserin, Diltiazem.

INTRODUCTION

Anal fissure is a vertical and painful ulcer in the anal canal extending between the linea dentata and the anal verge. Although it is usually observed in the posterior midline, it can also be seen in the anterior midline[1]. Despite the fact that anal fissure is observed at approximately the same rate in men and women of all age groups, it is is more frequently seen in young adults[2]. Anal fissures have both acute and chronic types according to their manifestations. While acute anal fissure appears as a sharp tear in the anal canal, chronic anal fissure is observed as a triad with the fissure itself, hypertrophied anal papilla in the proximal part and sentinal pili in the distal part. In addition, fissures with symptoms persisting longer than six weeks are considered chronic[3].

Anal fissures are thought to occur due to formation of a tear in the anoderm due to difficult, and traumatic defecation or prolonged diarrhea and increase in internal sphincter pressure due to the tear in anoderm, spasm and decrease in blood flow[4]. In general, severe pain during defecation, fresh blood smeared on feces and strenuous bowel movements are observed in patients with anal fissures[5]. Rectal discharge, tenesmus and itching are other presenting symptoms[4].

The aim in the treatment of chronic anal fissure is to reduce the pressure on the internal sphincter muscle and to weaken sphincter spasm and to increase local blood flow[6]. While the general tendency favours medical treatment in cases of acute anal fissure, surgical treatment is often preferred in the management of chronic anal fissures. Although different surgical techniques have been described, the most commonly performed surgery is lateral internal sphincterotomy (LIS), which is a complete or partial incision of the internal sphincter from the lateral side. LIS is the gold standard method in the treatment of chronic anal fissures[7]. Although surgery has been shown to have a high success rate in many studies, it is also known to cause undesirable results such as gas or fecal incontinence and abscess at the operation site[8]. For this reason, medical treatment approaches in chronic anal fissures have recently become more popular. Various therapeutic agents such as nitrates, calcium channel blockers, botulinum toxin have been proposed for chemical

sphincterotomy[9]. These medical treatment methods may be associated with gastrointestinal side effects such as headache, flushing, abdominal pain, nausea-vomiting, diarrhea and pruritus[10].

In the light of this information, we tried to retrospectively evaluate the surgically or medically treated cases of chronic anal fissures admitted to our clinic and to determine whether medical treatment can be an alternative to surgical treatment.

METHOD

A total of 136 patients who underwent medical or surgical treatment for their chronic anal fissures between June 2019 and December 2022 in the General Surgery Clinic of Balikesir University Hospital were retrospectively investigated. The study was approved by the clinical research ethics committee of Balikesir University (Date: 20.12.2023; Issue No: 2023/192). Preoperatively, informed consent was obtained from all patients who underwent surgical treatment. Patients over the age of 18 years were included in the study. Patients with fissures secondary to diseases such as inflammatory bowel disease, tuberculosis, malignancy, hemorrhoids and fistulas, mentally disabled patients, patients under 18 years of age and patients who had received previous treatment were excluded from the study. A total of 136 patients received either surgical (n:36; 26.5%) or medical (n.100; 73.5%) treatment. As medical treatment, patients received either topical glyceryl trinitrate (n: 54; 54%) or topical diltiazem (n:46; 46%). Patients using diltiazem were instructed to apply 2% of the topical preparation from the fingertip to the first joint of the their fingers for a length of approximately 2 to 2.5 cm twice a day , and insert this ointment about 1.5 cm into the anus. Patients using glyceryl trinitrate were instructed to apply 0.4% ointment twice a day 1-1.5 cm into the anus according to the measurement chart on the box. Topical treatment was applied for 8 weeks and patients were called for monthly controls. Surgically, patients who underwent lateral internal sphincterectomy (LIS) were called for monthly follow-up visits after discharge from the hospital. Complete healing was defined as the complete disappearance of the fissure by inspection in 8 weeks, while recurrence was defined as the re-occurrence of the fissure in patients with complete healing. Patients with complete healing were followed up for 6 months after termination of the treatment to search for the development of recurrence. Patients were evaluated in terms of age, gender, complete healing status, recurrence after complete healing, side effects and complications developed during treatment.

Statistical Analysis

In summarizing the data obtained from the study, descriptive statistics were tabulated as mean ± standard deviation or median, minimum and maximum depending on the distribution of continuous (numerical) variables. Categorical variables were summarized as numbers and percentages. The normality of the numerical variables was checked by Shapiro-Wilk, Kolmogorov-Smirnov and Anderson-Darling tests.

In comparisons of intergroup differences between categorical variables, Pearson chi-square test was used in 2x2 tables with expected value in each cell was ≥5. Fisher's exact and Fisher- Freeman - Halton tests were used in tables, and also RxC tables with expected value in each cell was less than[5]. In this study, logistic regression analyses were applied to determine the factors affecting recovery and recurrence after treatment in patients with chronic anal fissures, and the effect of variables on outcomes was analyzed using odds ratios (ORs), 95% confidence intervals (CI) and P values. These analyses were critical for understanding the efficacy of treatment modalities and the risk of recurrence. Statistical analyses were performed with Jamovi (Version 2.3.28) and JASP (Version 0.17.3) programs and the level of statistical significance level was set at 0.05 (p-value).

RESULTS

A total of 136 participants including 55 (40.4%) male, and 81 (59.6%) female patients with an

overall mean age of 36 years were enrolled in the study. Patients who received treatment were analyzed in three different groups as follows: surgery group (n:36; 26.5%), glyceryl trinitrate group (n:54; 39.7%), and diltiazem group (n: 46; 33.8%). Demographic characteristics, treatment modalities, complete cure/relapse and side effect/complication rates of all patients in all three groups are shown in Table I.

Table I: Demographic and clinical characteristics of all chronic anal fissure patients

	Overall (n=136)
Age (median: range) years	36.0 [18.0 – 73.0]
Gender ‡	
Male (n,%)	55 (40.4)
Female (n,%)	81 (59.6)
Groups ‡	
Surgery (n,%)	36 (26.5)
Topical glyceryl trinitrate (n,%)	54 (39.7)
Topical diltiazem (n,%)	46 (33.8)
Post-treatment status, *recovery* (n,%)	98 (72.1)
Recurrence during 6-month follow-up after complete healing (n,%)	13 (13.3)
Side effects/complications (n,%)	49 (36.0)
Distribution of side effects/complications	
Gas-fecal incontinence (n,%)	2 (4.1)
Perianal abscess (n,%)	2 (4.1)
Headache (n,%)	24 (49.0)
Gastrointestinal side effects (n,%)	18 (36.7)
Other (n,%)	3 (6.1)

When the demographic and clinical characteristics of chronic anal fissure patients were compared according to the treatment groups, no significant difference was observed between the groups in terms of age, gender, and recovery rates. The incidence of side effects and complications was significantly higher in patients receiving topical glyceryl trinitrate treatment ($p<0.001$). Gas/fecal incontinence and perianal abscess rates were significantly higher in the surgery group, and headache was reported at a significantly higher rate in the glyceryl trinitrate group compared to the other groups ($p<0.001$). There was no significant difference between the groups in terms of gastrointestinal system (GIS), and other side effects ($p>0.05$) (Table II). When the recurrence rates were evaluated according to the treatment groups in the 6-month follow-up of patients with chronic anal fissure who had complete recovery, no significant difference was observed between the groups in terms of recurrence rates ($p>0.05$) (Table II).

Table II: Comparison of demographic and clinical characteristics of chronic anal fissure patients according to treatment groups

	Groups			P
	Surgery (n=36)	Glyceryl trinitrate (n=54)	Diltiazem (n=46)	
Age (median, range) years	34.0 20.0 – 73.0]	36.0 [18.0 – 66.0]	36.0 [18.0 –64.0]	0.711**
Gender ‡				
Male (n,%)	15 (41.7)	24 (44.4)	16 (34.8)	0.609*
Female (n,%)	21 (58.3)	30 (55.6)	30 (65.2)	
Complete recovery after termination of the treatment (n,%)	31 (86.1)	35 (64.8)	32 (69.6)	0.079*
Recurrence rates of the patients with complete recovery (n,%)	2/31 (6.5)	7/35(20.0)	4/32 (12.5)	0.300*
Side effects/Complications, (n,%)	4 (11.1)	32 (59.3)	13 (28.3)	<0.001*
Distribution of side effects/complications				
Gas-fecal incontinence (n,%)	2 (5.5)	0 (0,0)	0 (0,0)	<0,001*
Perianal abscess (n,%)	2 (5.5)	0 (0,0)	0 (0,0)	
Headache (n,%)	0 (0,0)	18 (33.3)	6 (13.1)	
GIS side effects (n,%)	0 (0,0)	13 (24.1)	5 (10.8)	
Other (n,%)	0 (0,0)	1 (1.8)	2 (4.3)	

Statistical significance was evaluated using Pearson chi-square, Fisher- Freeman- Halton (*) and Kruskal -Wallis-H (**) tests.

DISCUSSION

Anal fissure is a common and painful disease of the anal canal. Although the etiology of this disease has still not been fully elucidated, it is thought to be caused by hypertrophy of the internal sphincter and increased anal sphincter resting pressure resulting in ischemia of the anoderm[4,11]. Although LIS is the most effective treatment method known in the management of chronic anal fissures, complications such as gas-fecal incontinence and wound infection may be encountered after LIS. Treatment of chronic anal fissures is still a controversial issue. Some studies suggest medical treatment methods as the first treatment option due to the non-invasiveness of these medical therapies and complications of surgical treatment such as gas-fecal incontinence[11]. Calcium channel blockers (diltiazem) and glyceryl trinitrate (nitric oxide derivatives) are commonly used for medical treatment. The these treatments are applied with the aim to reduce sphincter tone, relieve pain and heal the fissure[11,12]. A total 136 participants including 55 (40.4%) male, and 81 (59.6%) female patients with an overall mean age of 36 years participated in our study. Demographic characteristics similar to our study are also observed in the literature. In a meta-analysis of randomized controlled trials, anal fissure was observed more frequently in women with a rate of 54.9%; and in another publication, it was seen more frequently in young and middle-aged patients[6,13].

Many studies have reported varying degrees of efficacy of chemical sphincterotomy using topical glyceryl trinitrate and calcium channel blockers and surgical sphincterotomy. Brown et al. examined 82 patients who received surgical or medical treatments due to chronic anal fissures and found that surgery was superior to applications of glyceryl trinitrate and calcium channel blockers in terms of healing[14]. In a prospective randomized controlled study with a total of 90 patients,Vaithianathan et al. also reported higher healing rates in patients treated with LiS than diltiazem application[3]. Ameta-analysis of 9 randomized controlled studies arrived at a conclusion that topical diltiazem and glyceryl trinitrate had similar healing rates[15]. In our study, similar to the literature data, complete recovery was found at a higher rate in patients who underwent surgery (surgery group: 86.1%; glyceryl trinitrate group: 64.8%; diltiazem group: 69.6%); however, without any statistically significant difference between the treatment groups in terms of complete recovery. We think that this lack of statistically significant intergroup difference stems from lower number of patients who underwent surgery when compared to other treatment groups.

Many side effects and complications may be observed during surgical or topical treatment of chronic anal fissures. In the study by Patel et al. gas incontinence was observed in 3.4% of the patients and fecal incontinence in 3.4% of the patients after LIS[16]. Acar et al. found gas incontinence in 1%, fecal incontinence in 1% and postoperative anal abscess in 1% of the patients who underwent LIS[17]. In our study, postoperatively, gas and fecal incontinence was found in 5.5% and anal abscess in 5.5% of the patients. Gas or fecal incontinence and perianal abscess were not observed in patients who received topical treatment.

In a study comparing the side effects of topical glyceryl trinitrate and diltiazem applications in the treatment of chronic anal fissures, headache and gastrointestinal side effects were observed at a higher rate in the glyceryl trinitrate group[10]. In our study, we observed headache and gastrointestinal side effects at a higher rate in patients receiving topical glyceryl trinitrate than in patients using diltiazem ointment in accordance with the literature data. Gastrointestinal side effects including nausea, vomiting and diarrhea (n:13; 24.1%) and headache (n: 18;33.3.%) were observed in

patients using topical glyceryl trinitrate. Urticaria-like manifestations were observed in one (1.8%) patient. Headache was observed in 6 (13.1%) and gastrointestinal side effects in 5 (10.8%) patients who used diltiazem ointment In 2 patients (4.3%), urticaria-like manifestations and arrhythmia were observed. However, none of the side effects were serious enough to interrupt the treatment. Headache and gastrointestinal side effects were not observed in patients who received surgical treatment.

The most effective treatment modality with the lowest risk of posttreatment recurrence should be preferred in the management of chronic anal fissures. Many studies cited in the literature have evaluated the development of recurrence in patients who recovered after surgical or topical treatment. Recurrence rates after surgery vary between approximately 3-11% in the literature[18–21]. Shrivastava et al. reported recurrence rates as 33% in the glyceryl trinitrate group and 13.3% in the diltiazem group[22]. Bansal et al. found a recurrence rate of 11.1% in the glyceryl trinitrate group and 15% in the diltiazem group[23]. In our study, recurrence rates were 6.5% (n:2) in the surgical treatment, 20% (n:7) (in the glyceryl trinitrate group and 12.5% (n.4) in the diltiazem group after 6 months of follow-up without any statistically significant intergroup difference.

While the relatively small number of patients in the treatment groups, along with its retrospective nature and single-center design, are limitations of our study, this research has demonstrated that topical treatments may serve as alternatives, particularly in patients who refuse surgical intervention for chronic anal fissures.

CONCLUSION

Our study has revealed that although any statistically significant difference between treatment modalities was not observed, higher recovery, and lower recurrence rates were achieved after surgical treatment when compared to other treatment methods. However, surgery is the most vulnerable method to complications such as incontinence and abscess. Since the side effects or complications that may develop are also decisive in choosing the treatment method, topical diltiazem therapy, which has fewer complications compared to other medical treatment methods, has yielded outcomes similar those obtained with other treatment methods in terms of recovery and recurrence rates, we think that in the treatment of chronic anal fissure, especially in patients who are afraid of complications of surgery such as gas or fecal incontinence, and in patients who do not benefit from this treatment or who cannot adapt to medical treatment, lateral internal sphincterotomy will increase the success and reduce the complication rates. Surgical intervention stands as the foremost efficacious approach for addressing chronic anal fissures; however, in cases where patients decline surgery due to undesirable side effects, topical treatments present themselves as viable alternative

We think that prospective, randomized controlled studies with a higher number of patients will more clearly show the efficacy of topical treatments in the treatment of chronic anal fissures and the relevant rates of improvement and recurrence.

Ethics Committee Approval: The study was approved by the clinical research ethics committee of Balikesir University (Date: 20.12.2023; Issue No: 2023/192).

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