



## RESEARCH ARTICLE

### A NEW AND EFFECTIVE TOPICAL TREATMENT METHOD IN CHRONIC ANAL FISSURE AND ITS COMPARISON WITH SURGICAL TREATMENT

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#### ABSTRACT

**Objectives:** Chronic anal fissure is one of the most common disorder in the anal region. In the treatment, surgical methods and topical treatments are used together or as a single. In this study, we aimed to investigate the effectiveness of a new medical topical treatment combination and its comparison with lateral internal sphincterectomies in chronic anal fissure.

**Materials and Methods:** A total of 144 chronic anal fissure patients, were divided into two groups. In the topical medical treatment group, a topical cream mixture that includes bacitracin, neomycin sulfate, neomycin, diltiazem, dexapanthenol was applied in the anal region in 82 patients. In the surgery group, 62 patients underwent surgery. After the treatment, defecation pain scores, stool bleeding, healing, gas-fecal incontinence, treatment-related side effects were evaluated in two groups.

**Results:** Recovery rates were higher in the surgical treatment group (93.5%) according to the topical treatment group (82.9%). The visual analog pain scores were higher in the surgical group too. But gas-fecal incontinence ratio, severity of pain with defecation were significantly different as supporting the medical treatment.

**Conclusion:** We would like to underline that of medical treatment in patients with chronic anal fissure can be applied before surgical treatment.

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## INTRODUCTION

Chronic anal fissure is a painful disorder of anal region with an unknown etiology. Chronic constipation in patients results with painful defecation of hard stool in the rectum, cause trauma in the anal region and secondary to trauma, chronic fissures are formed (Othman, 2010; Puche et al., 2010). These fissures secondary to trauma with hard defecation, create pain in the anal region and this pain related anal sphincter tone is increasing. Also increasing anal sphincter tone can cause ischemic ulcers (Gibbons and Read, 1986; Schouten et al., 1994). Ischemia is the mostly blamed pathology for the mechanism of anal fissure. Because of this, agents that can diminish ischemia such as ozone may heal anal fissure (Isik et al., 2015). In the literature the most effective treatment of chronic anal fissure shown as lateral internal sphincterectomy (LIS) (Nelson, 2005). However gas and fecal incontinence are the disadvantages of lateral internal sphincterectomy (Nyam and Pemberton, 1999). Alternative to surgical treatment, sphincter pressure-lowering treatments can be used. Some of the chemicals are used for this purpose (temporarily sphincterotomy forming drugs), drugs that increase the amount of nitric oxide and calcium channel blockers

(Arroyo et al., 2005). Ordinarily, the purpose for the use of topical agents is to reduce chronic anal fissure anal sphincter tone. But fissure is a chronic wound and has problems such as infection and epithelialization. The aim of this study was to find effective topical mixture to treat chronic anal fissure by adding antibacterial and epithelializing agents. In this direction, we used a topical mixture treatment to lower sphincter pressure; diltiazem, bacitracin-neomycin as antibacterial and the dexapanthenol causing epithelialization were combined. It was designed by Hasan Borekci. The topical efficacy of this treatment was evaluated by comparing the lateral internal sphincterectomy.

## MATERIALS AND METHODS

For this study, ethics committee approval was taken at Bozok University Ethics committee (approval number: 05/08/2013-152). In addition, patients were informed about the treatment and study, informed consents were taken. 165 patients included to study with the diagnosis of anal fissure in one year period. All of the patients in this study had complaints due to chronic anal fissure at least 8 weeks; such as difficulty in defecation, bleeding during defecation and all had one fissure on the posterior of the anal region and sentinel pili. Patients having multiple fissures in the anal region, in addition to anal fistula or hemorrhoids, malignancies and the failure of the treatment;

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these cases were excluded from the study. Study designed as randomized and progressive. All of the patients were informed on the means of medical and surgical treatment and included to study group according to their wish as medical group (n=82) and surgical group (n=62) after excluding the non-follow up patients. The surgical group patients were treated with open technic lateral internal sphincterectomy and discharged with warm dressing and 2x1 oral 500 mg Cefuroxime axetil (Cefaks tablet; Deva Drug Endustry, Istanbul, Turkey). Patients were invited for follow-up clinical control in postoperative 1 week and 60 th day. We prepared the topical mixtures: In the chronic anal fissure treatment, reducing the sphincter pressure is the classical sense, so that we put diltiazem (Diltizem tablet, Mustafa Nevzat Drug Endustry, Istanbul, Turkey) in the mixture as it is a calcium channel blocker. In addition, we added easily available local antibiotics bacitracin and neomycin (Thiocilline; Abdi Ibrahim Drug Endustry, Istanbul, Turkey) as it is a chronic wound (Schalock and Zug, 2005). Chronic anal fissures are chronic wounds and their epithelization is so difficult, therefore we also used dexapanthenol (Bepanthen cream; Bayer HealthCare, Leverkusen, Germany). We believe that dexapanthenol is effective on closure of wound earlier. (Wollina, 2005). In the topical mixture there were following drugs;

- 15000 IU bacitracin-150 mg neomycin sulfate containing 105 mg of neomycin base (in 30g tubes)-1500 mg dexapanthenol (in 30 g tubes)
- 30 mg tablets of diltiazem (in 1 box there are 48 tablets and whole box was used) So the topical mixture cream formed by 15000 UI bacitracin
- 150 mg neomycin sulfate containing 105 mg of neomycin base
- 1500 mg dexapanthenol and 1440 mg diltiazem.

We crushed the diltiazem tablets and then put into the mixture. The topical cream was applied as 1 cm<sup>3</sup> amount, 3 times a day for 6 weeks on the anal region in the medical group. Although many of the complaints of patients had decreased within the first 2 weeks. We continued treatment for about 6 weeks. After 60 days of treatment initiation, both groups were examined to understand the fissure healing and these questions were asked;

- Whether there is pain on defecation. The visual pain scale was used. They gave up points from 0 to 9 according to the severity of pain. As without pain (0), for those with mild pain (score 1-5), for those with severe pain (score 6-9) (Agrawal *et al.*, 2013).
- Whether there is bleeding in defecation (1: yes-0: none).
- Treatment-related side effects. All patients examined whether fissure line epithelialized. (1: there is healing/being epithelialized - 0: no healing)

### Statistical analysis

The statistical analyses were performed using software SPSS 16.0 (SPSS Inc., Chicago, IL, USA). The Shapiro-Wilk's test was used and histogram and q-q plots were examined to assess the data normality. Accordingly, Mann-Whitney U test was used to compare the differences of continuous variables between groups. Chi-square analyses were used to compare the differences of categorical variables. A P < 0.05 probability level was considered as statistically significant.

## RESULTS

The demographic and clinical characteristics of both two groups are summarized in Table 1. Gender and age did not differ between the two groups. In the medical treatment group 48 (58.5%) of female and 34 (41.5%) of were male. In the surgical treatment group 26 (41.9%) of female, 36 (58.1%) of were males. Mean age was 37.4 ± 13.3 in the medical treatment group and 32 ± 12.4 in the surgical group (Table 1). In the postoperative 60<sup>th</sup> day evaluation, according to the visual pain scale; patients without pain (score 0) and with mild pain (score 1-5) were compared both in two groups, and there was no statistically significant difference between the medical therapy group and the surgical treatment group (P > 0.05). Patients with painful defecation (score 6-9) were evaluated; 14 (17.1%) patients in the medical therapy group and 2 (3.2%) in the surgical treatment group (3.2%) had severe pain (P = 0.015) (Figure 1). In the medical therapy group, 16 of them had sometimes bleeding after treatment and 6 of surgical treatment patients had bleeding after defecation (P = 0.104) (Table 1).

**Table 1. The basic characteristics of the patients with chronic anal fissure**

	Topical Treatment group (82 patient)	Surgical treatment Group (62 patient)	P
<b>Gender:</b>			
1.male	34(41.5%)	36(58.1%)	0.048
2.Female	48 (58.5%)	26(41.9%)	
<b>Age</b>	37.4±13.3	32±12.4	0.087
<b>Visual pain score</b>			
1-No pain in defecation (0)	28(34.1%)	27(43.5%)	0.015
2-Mild pain (1-5)	40(48.8%)	33(53.2%)	
3-Severe pain (6-9)	14(17.1%)	2(3.2%)	
Bleeding after defecation	16(19.5%)	6(9.7%)	0.104
Gas – fecal incontinence	0(0%)	4(2.8%)	0.020
Headache	0(0%)	6(9.6%)	0.004
Itching in Anal area	4(4.8%)	0(0%)	0.078
Redness in Anal area	2(2.4%)	0(0%)	0.216
Recovery	68(82.9%)	58(93.5%)	0.056

Data are expressed as mean ± SD, number (percentage)

The medical treatment group had no gas fecal incontinence, but in the surgically treated group 4 (2.8%) of had temporary gas fecal incontinence (P = 0.020). After 60 day, there wasn't gas fecal incontinence in surgery group. When treatment side effects determined; in the surgical treatment group 6 (10%) of complained of headache due to the spinal anesthesia, but there was no headache in medical therapy group (P < 0.05) (12). We recommended fluid intake and additional parasetamol and caffeine containing analgesic tablets daily to patients with headache and within 15 days headaches improved. In addition, in the medical treatment group, 4 of had itching, 2 of patients had redness (allergic reaction) in anal region. Itching and allergic reaction was missed 7-10 days later the treatment by itself. In the surgical treatment group there was no redness or itching in the anal region (P > 0.05). There wasn't any complication like abscess after LIS. The recovery rate was 82.9% (68 patients) in the medical treatment group, and 93.5%

(58patients) in the surgical treatment group ( $P = 0.056$ ) (Figure 2).

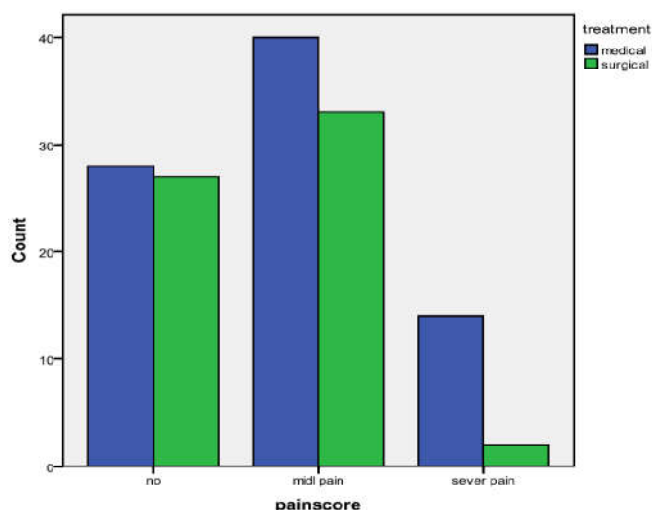


Figure 1. Visual pain scale of both medical and surgical treatment group

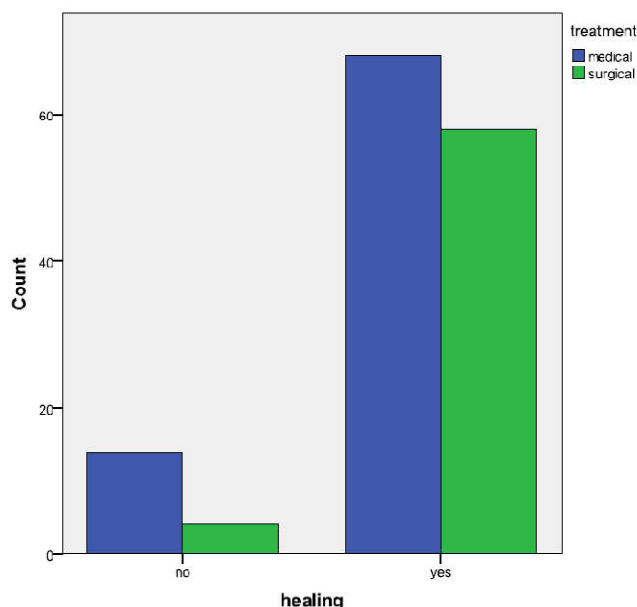


Figure 2. The recovery rate of both medical and surgical treatment group

## DISCUSSION

In the treatment of chronic anal fissure, anal sphincter pressure lowering treatment is the main basis of the therapy. In this study, thinking that chronic anal fissure is a chronic infected wound, were compared combined medical therapy effectiveness (reducing anal sphincter pressure and local antibiotics for the chronic wound healing and agents forepithelization) with surgical treatment (Park *et al.*, 2013). One of the main factors in chronic wound healing is: to clean wound from infection agents and to facilitate the wound epithelialized (Wilasrusmee *et al.*, 2013). For this purpose, diltiazem was used to reduce the pressure in the anal sphincter pressure, bacitracin-neomycin as an antibiotic, dexapanthenol for epithelization. These antibiotics bacitracin and neomycin are commonly used as topical agents in infected wounds and easy to reach and well-tolerated agents. Perhaps in future other antibacterial agents will be able to use in chronic anal fissure. In

the study of Pucher *et al.* 2010 on 39 patients treated with diltiazem; they stated the recovery rate as 46% (18 patients) (2). In the study of Kennedy *et al.*, 1999 gliseriltrinitrat 2% (GTN) has been compared with the placebo group and there was 46% recovery in GTN group and 16% in the placebo group (15). In the study of Jones *et al.*, 2002 after 8-week study with glyceroltrinitrate there was no recovery and because of resistance to therapy they used diltiazem and recovery rate was 48% (Jones *et al.*, 2002). Knight *et al.*, 2001 used topical diltiazem in 71 patients with chronic anal fissure and recovery rate was 83% (Knight *et al.*, 2001; Medhi *et al.*, 2011). The recovery rate was 82.9% in our study in the topical medical treatment group. When we compare with the other studies we can state that our recovery rate is high although 17.1% of patients complaints did not improve and, fissure line not cured. We saw few side effects in the medical treatment group and itching, redness complaints end within 7-10 days so we can say that it is a tolerable therapy. We compare the recovery rate in two groups. Medical treatment is as effective as surgical treatment ( $P > 0.005$ ). Although surgical treatment is a highly effective method for patients it can cause persistent problems such as gas fecal incontinence and these complaints can not be ignored. In a study with 29 patients; all patients underwent open lateral internal sphincterectomy. One (3.4%) has gas incontinence and 1 (3.4%) has fecal incontinence after the surgery. Although it seems low, these incontinence problems effects the quality of life seriously (Patel *et al.*, 2013). In our study, gas fecal incontinence was determined in 2.8% of patients after surgery and this result was parallel to the literature data. In the surgical treatment group with spinal anesthesia some complications can be seen but in the topical therapy there are no complications and this increases the priority and the effectiveness of treatment. Placer and his colleagues study on chronic anal fissured patients; medical topical treatment applied for about 8 weeks but in our study, topical mixture was used for 6 weeks (Placer *et al.*, 2007). Total of 100 patients were treated with topical 2% diltiazem and the recovery rate was 62% and 5% of their patients morbidity continued.

The recovery rate in the study of Placer seems high (Placer *et al.*, 2007). We believe that bacitracin and dexapanthenol which we added to the diltiazem increased our recovery rate up to 82.9%, 2.4% rate of diltiazem was used in the mixture and this is higher than used in many studies (2% used in studies) (Shah *et al.*, 2013). We believe that this high rate also contributes to the high rate of recovery. High dose of diltiazem may relax the anal sphincter longer. In addition, diltiazem can cause headache but in our group we did not see this side effect (Jonas-Obichere *et al.*, 2005). Calcium channel blockers (diltiazem) has anal sphincter spasm-reducing effects and believed to have a major effect on the healing of fissures. In our study, 72 patients were treated with topical mixture, 4 (4.8%) of them had itching, 2 (2.4%) of allergic reaction in the anal region. We think that these side effects may belong to diltiazem and there are studies in the literature supporting this data (Wong and Horn, 2010). In our study, we saw that these allergic side effects did not disturb too much the quality of life of the patients and missed in a short time. The fissure localization of our patients were the anorectal posterior wall and only one fissure in all patients. This patient selection makes our results more reliable and sensitive. We investigated the efficacy of combine treatment which we prepared. These agents (bacitracin-neomycin-dexapanthenol) may be tried separately in other studies and specific roles of each agent can be investigated. Because of this and similar studies; separately or combine effects of these drugs

can be determined and also if they reduce or increase the effects of each other. We might have compared our topical mixture with another topical therapy but we know that the lateral internal sphincterectomy is the most effective method in chronic anal fissure. We think that comparing medical and surgical treatment is more reliable when evaluating recovery rates. As a result we can say that this topical mixture we prepared is very effective in treating chronic anal fissures. Although the recovery rate is not superior to surgical treatment and we have not recurrences rates in the study. Medical treatment has some advantages such as local administration, high recovery rate, less pain in defecation and no complication risk of the surgery. It also will not prevent surgical treatment after medical application. Patients who failed medical therapy can be taken immediately to surgery. Based on these results this topical treatment can be preferred in chronic anal fissure. We can say that this medical therapy in patients with chronic anal fissure can be useful and worth to try before surgical treatment. In our study, there are not any conflict of interest and financial disclosure.

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