Comparative assessment of effectiveness of combination therapy with 7% Sucralfate and 2% Diltiazem versus 2% Diltiazem alone in treatment of chronic anal fissure – randomized prospective study

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OCENA PORÓWNAWCZA SKUTECZNOŚCI ŁĄCZONEJ TERAPII 7% SULCRALFACTEM Z 2% DILTIAZEMEM W PORÓWNANIU Z LECZENIEM SAMYM 2% DILTIAZEMEM W LECZENIU PRZEWLEKŁEJ SZCZELINY ODBYTU – RANDOMIZOWANE BADANIE PROSPEKTYWNE

Streszczenie

Wstęp. Szczelina odbytu jest obok choroby hemoroidalnej najczęściej występującą proktologiczną chorobą zapalną. Ze względu na możliwość komplikacji po operacji szczeliny w postaci objawów inkontynencji, aktualnie podstawowym leczeniem jest leczenie zachowawcze. Niniejsza praca stanowi propozycję terapii łączonej, wykorzystującej działania Diltiazemu i Sulcralfatu. Diltiazem (bloker kanałów wapniowych) obniża napięcie mięśni zwieraczy, podczas gdy Sulcralfat ma działanie gojące anodermę.
Cel pracy. Ocena porównawcza skuteczności łączonej terapii 7% Sulcralfactem z 2% Diltiazemem w porównaniu z leczeniem samym 2% Diltiazemem w leczeniu przewlekłej szczeliny odbytu.
Materiał i metody. 46 pacjentów (30 kobiet, 16 mężczyzn) w wieku od 22 do 80 lat (śr wieku 44,6 lat) z przewlekłą szczeliną odbytu: 21 pacjentów leczonych Diltiazemem podawanym 2 x dziennie doodbytniczo w postaci 2% maści, 25 pacjentów leczonych Diltiazemem oraz 7% maścią z Sulcralfatu (Diltiazem 1 x dziennie, Sulcralfat 1 x dziennie) przez 8 tygodni. Podczas pierwszej wizyty oraz wizyty kontrolnej po 8-10 tygodniach leczenia oceniano dolegliwości pacjenta w skali bólu werbalnej i wizualnej oraz pacjent był badany proktologicznie.
Wyniki. Zagojenie szczeliny stwierdzono u 15 z 21 pacjentów (71,5%) leczonych samym Diltiazemem oraz u 21 z 25 pacjentów (84%) leczonych Diltiazemem i Sulcralfaktem. Różnica nie była istotna statystycznie W żadnym przypadku nie stwierdzono działań ubocznych zastosowanych leków.
Wnioski. Terapia łączona 2% Diltiazemem z 7% Sulcralfatem okazała się skuteczniejszą metodą leczenia przewlekłej szczeliny odbytu w porównaniu z leczeniem szczeliny samym 2% Diltiazemem w badanej grupie pacjentów. Różnica nie była istotna statystycznie. Powyższy wniosek wymaga potwierdzenia na większej grupie pacjentów.

Słowa kluczowe: szczelina odbytu, sulcralfat, diltiazem, chemiczna sfinkterotomia

INTRODUCTION

Anal fissure together with haemorrhoidal disease are the most often occurring inflammatory proctological diseases. According to reference books, approximately 15% of proctological consultations concerns patients with anal fissure (1). Because of potential complications after surgery of anal fissure in the form of symptoms of incontinence, currently the primary treatment is non-invasive treatment. This paper proposes a combination therapy, using Diltiazem and Sucralfate. Diltiazem (calcium channel blocker) reduces tension of sphincter muscles, while Sucralfate has a healing effect on anoderm.

Diltiazem is a calcium pump inhibitor in the muscles and, at the same time, a preparation that dilates blood and improves blood circulation in tissues. For several years, it has been often used in treatment of anal fissures, because it acts indirectly on relaxation of the internal sphincter muscle and helps heal the fissure (2-5). Preparations that decrease tension in the internal sphincter muscle improve blood circulation in tissues and facilitate the outflow of inflammatory anal discharges. Calcium channel blockers are used in treatment of anal fissure, wound healing after hemorrhoidectomy and, locally, into the anal canal to reduce pain in patients after various proctologic surgeries (6).

Sucralfate, in turn, is a medicine used in treatment of ulcer disease. In proctology, its beneficial therapeutic effect is described in the context of solitary rectal ulcer

treatment (7-9). It provides local effects and accelerates healing. Recently a few reports have been produced on the effectiveness of sulcralfat in treatment of other types of diseases, such as anal fistula (10, 11). 7% Sucralfate in ointment is applied topically twice a day for 6 weeks into the anal canal, into fistulotomy wounds, and after hemorrhoidectomy. Due to the different and yet complementary mechanism of action of these preparations, the authors decided to combine the action of both medicines in patients with chronic anal fissure.

MATERIAL AND METHODS

46 patients (30 women, 16 men) aged 22 to 80 years (mean age 44 years) with chronic anal fissure.

Exclusion criteria: ailment lasting at least 3 months.

Exclusion criteria: inflammatory bowel disease, anal fissure surgery, pregnancy.

Group I: 21 patients treated with 2%Diltiazem administered twice a day into anus in the form of 2% ointment.

Group II: 25 patients treated with 2% Diltiazem and 7% Sucralfate ointment (Diltiazem once a day, Sucralfate once a day) for 8 weeks. During the first visit, and the follow up visit after 8-10 weeks of treatment, the patient was examined proctologically, per rectum, and underwent an anoscopy procedure. The ailments of the patient was measured on a scale of verbal and visual pain (VAS scale). Verbal assessment scale evaluated pain from 0 to 3 points: 0 meant no pain, 1 slight pain, 2 strong pain, 3 unbearable pain. The visual scale evaluated pain from 1 (no pain) to 10 (unbearable pain). The assessment took into consideration the effectiveness of treatment and side effects.

Statistical method used: Chi-squared test.

RESULTS

Healing of anal fissure occurred in 15 of 21 patients (71.5%) from Group I treated with Diltiazem alone and in 21 of 25 patients (84%) from Group II treated with Diltiazem and Sucralfate. No adverse effects of used medications were noted.

Statistical analysis: Chi-squared test.

The p value is 0.303172. This result is not significant at $p < 0.05$.

The difference turned out not to be statistically significant.

DISCUSSION

The efficacy of calcium channel blockers in the treatment of anal fissure has been described for several years (2-5). Previous observations by other authors are confirmed in the presented study, where the percentage of successful treatment of chronic anal fissure with Dilitiazem alone amounted to 71.5%. Given the fact that the fissure is a type of wound in the anal canal, therapy with diltiazem complemented with local treatment with Sucralfate has its logical explanation. Diltiazem reduces tension of sphincter muscles, while Sucralfate has a healing effect on anoderm. The efficacy of combination therapy in the treatment of chronic anal fissure proved greater than the diltiazem (71.5% versus 84%). The difference was not statistically significant.

Anal fissure, except postpartum fissure, is always associated with increased sphincter muscle tension. The beneficial effects of Diltiazem includes reduction of tension of these muscles. In own study comparing topical action of Diltiazem and nitrates, similar efficacy of both medicines was found, while nitrates produced a higher percentage of side effects (headache) (2). The beneficial effect of nitrates on blood supply of the anal canal and on the healing of fissure was described by other authors (12, 13). However, the authors of this article rarely use nitrates in fissure treatment, due to unpleasant side effects for the patient, including headaches. Much more often, they administer Diltiazem in 2% ointment. Complementary treatment with Sulcralfat was to accelerate the topical healing process of anoderm.

6 patients in the first group and 4 in the other were qualified for surgery due to lack of improvement while undergoing the conservative treatment. Most surgeons agree with the fact that if the fissure does not heal or if a surgeon raises doubts as to the etiology of the fissure (cancer, Crohn's disease), histopathological examination sould always be performed.

The advantage of this method of treatment is the lack of side effects, although the studied patient group was small and the optimistic conclusions on the presented method of treatment would require confirmation in a larger group of patients.

This work is yet another alternative to conservative treatment, combination therapy, using therapeutic effects of both medicines. There are no side effects and a high success rate of this therpay is an advantage of the method.

CONCLUSIONS

A combination therapy with 2% Diltiazem and 7% Sulcralfat oinments is an effective method of chronic anal fissure treatment and is more effective than treatment with 2% Diltiazem alone. This result is not significant. This conclusion needs to be confirmed on a larger group of patients. □

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