Establishing the Superiority of Topical Diltiazem Over Compound Cream in the Treatment of Chronic Anal Fissure: A Prospective Analytical Study

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ABSTRACT:

BACKGROUND:

Anal fissure is an elliptical ulcer in the anal canal extending from the dentate line to the anal verge; chronic anal fissure is a common problem across the world treated largely by surgical methods. The treatment for chronic anal fissure (CAF) has undergone a transformation in recent years from surgical to medical as the common goal is reducing the internal anal sphincter spasm.

OBJECTIVE:

To assess the efficacy of topical treatment with 2% diltiazem gel (DTZ) in patient with chronic anal fissure versus combination cream.

MATERIAL AND METHODS:

Consecutive 400 adult male patients with symptomatic chronic anal fissure attending the surgery clinic were enrolled in the study form February 2014- July 2016, 200 patients were treated with topical application of 2% DTZ cream, other 200 patients were treated with combination cream. Patients were followed up for 6 month at regular intervals for symptomatic relief and healing of fissure.

RESULT &CONCLUSION:

In our study diltiazem 2% gel was more effective than combination cream in the treatment of chronic anal fissure.

KEYWORDS: chronic anal fissure, combination cream, diltiazem gel.

INTRODUCTION:

Anal fissure is an elliptical ulcer in the anal canal extending from the dentate line to the anal verge. It is associated with hypertonia of the internal anal sphincter (IAS) and pain.[1] An anal fissure is likely to be non-healing if the fissure persists beyond 4 week, a chronic fissure can be identified by the presence of indurated edges, visible internal sphincter fibers at the base of the fissure, a sentinel polyp at the distal end of the fissure or a fibroepithelial polyp at the apex. A chronic fissure classically occurs at the posterior midline position (6 o'clock position), with the anterior midline position occurring in 10% of females and 1% of males.[1,2] The vicious cycle of pain and spasm of IAS leads to reduced mucosal blood flow with microcirculatory disturbance, hence to poor healing of the fissure and a poor healing tendency will affect fissure healing.[3] The definition of chronic anal fissure is a combination of morphological and chronological aspects; chronic anal fissure is a common problem across the world treated largely by surgical methods. The treatment for chronic anal fissure (CAF) has undergone a transformation in recent years from surgical to medical Chemical sphincterotomy (This term refers to pharmacological manipulation of anal sphincter tone to induce a temporary reduction of anal canal pressure to promote healing of the fissure without permanently disrupting normal sphincter function) for reduction in anal sphincter tone which is achievable by enhancing IAS relaxation through direct action on internal anal sphincter smooth muscle cells.[4,5] Both the approaches share the common goal of reducing the IAS spasm. Surgical options for treating chronic anal fissures (lateral internal sphincterotomy and fissurectomy) are significantly more effective than all of the medical options. However, as the surgical options are associated with an increased risk of irreversible incontinence, they are usually only tried after medical options have been exhausted. Conservative treatment of anal fissures includes topical application of combination creams (corticosteroids, local anesthetics, rubefacient and astringent materials) with high success rate.[6,7] Studies have demonstrated the efficacy of topical agents like

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Glyceryl Trinitrate (GTN) in anal fissure but it has been shown to have side effects like headache and dizziness which are significantly less with diltiazem 2% gel which act by mechanisms serves to reduce intracellular Ca2+, which reduces the tonic state of the muscle. Hence there is a need for a pharmacological therapy for fissure which has fewer side effects.[8-11]

This study was taken up to assess the efficacy of topical 2% Diltiazem (DTZ) gel versus combination creams world wide known for the treatment of anal fissure which consist of corticosteroids, local anesthetics, astringent and rubefacient; commercially known proctocinolone; which is composed of fluococinolone acetonide 100mg, lidocaine HCl 20 mg, bismuth subgallate 50 mg and menthol 25 mg consecutively. Fluococinolone acetonide is a corticosteroid used to decrease inflammation locally; lidocaine is a local anesthetic agent to reduce pain and while bismuth subgallate is a dermatological, antiseptic disinfectant and astringent agent. Menthol is a topical rubefacient that produce an increase in blood circulation by dilatation of the superficial capillaries also sometimes been used to relieve acute on chronic pain. Both methods of management follow the basic management lines which includes, advice to increase fluid and high fiber meals intake and use of bulking agents to reduce resting anal canal pressure, lubricating laxatives oral emulsion to reduce straining and prevent constipation, if all of these with DTZ 2% gel or combined cream fail to heal for 6-8 weeks then consider that patient as a non-responder and shift to surgical Lateral internal Sphincterotomy as many studies depend on.[10-15]

AIM:

Anal fissures are associated with hypertonia of the internal anal sphincter and pain. We evaluated the efficacy of local application of both DTZ 2% gel and combination cream in the healing of chronic anal fissure.

METHODS:

In this prospective, randomized study, 400 male patients with chronic anal fissure were recruited to full fill the criteria of the study; which include males who had commitment for follow up period of 6 months with a two weeks visit to the surgical clinic and not to stop treatment during first 6-8 weeks. Patients having anal fissure due to other diseases such as inflammatory bowel disease, tuberculosis, malignancy, or STD, those who had taken prior course of topical agents, and those who had undergone surgery for anal fissure in past, those having associated hemorrhoids or fistula, patients with significant cardiovascular conditions, immune compromised and diabetics, were not included in the study.

Patients were educated to apply gel or cream internally in the anus and around the anal verge by squeezing the diltiazem 2% gel or the cream onto a finger and to apply this inside the anus and around the anal margin. Each patient was given a 6-8 weeks course of treatment with a twice-daily application, as close to every twelve hour as possible. Objective changes were assessed by the inspection of the anus to determine the extent of fissure healing (recorded as “healed” or “persistent”) at second, fourth, sixth and eighth weeks visits. Anoscopy was performed at baseline, sixth and eighth weeks. Healing of chronic anal fissure was defined at anoscopy when epithelialization or formation of a scar was achieved at week 6 or 8 of therapy. Then follow patients for the rest of the period for relapse at which repeat of the treatment course was done for another 6-8 weeks included I the follow up period; patients not responding after 8 weeks of treatment were shifted to surgical method (non responders). 200 Patients received local applications of DTZ 2% gel, and the other 200 patients received combination cream. Healing of anal fissure at 6 month follow up period was done and used as the end-point of the study period. Patients were carefully selected as to decrease bias in this study; patients must not have any other comorbidity factors that can indent the healing ability of the patients. Patients were educated about their disease and advised to have hot water bath sits (to increase blood flow to are), hallow sitting seats (help to reduce pressure and pain on the anosacral region), advice to increase fluids and high fiber meals intake with the use of bulking agents (to reduce resting anal canal pressure), lubricating laxatives oral emulsion (to reduce straining and prevent constipation), decreasing sitting times especially on hard based sits and not to prolong toilets sits.[4,18]

RESULTS:

Rates of complete healing of chronic anal fissure were different in the two groups when comparing the therapies between each other; preferable treatment regime could be found with DTZ 2% gel than with combined cream as shown in the table 1.

Table 1: Healing and non-responding patients to DTZ 2% and combination cream treatment.

Treatment	Patients No.	Healed	Non responder
Diltiazem gel 2%	200	162 (81%)	38 (19%)
Combination cream	200	114 (57%)	86 (43%)

While the relapsing rates to treatment during the 6 months follow up period were more with combination cream than with the DTZ 2% gel as shown in table 2.

Table 2: Relapsing rates to DTZ 2% gel and combination cream.

Treatment	Patients No.	Non relapsing	Relapsing
Diltiazem 2% gel	162	114 (71%)	48 (29%)
Combination cream	114	16 (14%)	98 (86%)

DISCUSSION :

Fissure-in-ano is a common problem across all parts of the world, causing considerable morbidity and affecting the quality of life of the patients. This necessitates the prompt treatment of the condition with suitable, cost-effective methods.[4,5,6]

DTZ gel helps in faster healing of anal fissures and provides better symptomatic relief than combined cream with better non-relapsing rates. Diltiazem gel 2% applied topically twice daily to and around anal fissures (for up to 8 weeks) works by reducing intracellular calcium in smooth muscle, relaxing the internal anal sphincter (chemical sphincterotomy).[19,20]

Studies included in a Cochrane review (2012) show superiority of topical diltiazem to placebo (80% vs 33%healing in 8 weeks respectively), and similar efficacy to topical glyceryl Trinitrate, but with reduced frequency of adverse effects.[21] In a study carried out by Knight et al., 71 consecutive patients with CAF were treated with DTZ (2%) ointment for 9 wk. About 88% of patients healed with DTZ ointment. Four patients experienced perianal dermatitis and one patient suffered from headache. After 32 wk. completion of the treatment, 27 of 41 patients available remained symptom-free. Six of the seven patients with recurrent fissure were treated successfully by repeating DTZ treatment.[22] In yet another study, patients with CAF were treated topically with 2% DTZ gel (dose 8 mg) three times daily. Twenty-three patients (12 women) with median age 45 yr. had a median 6 months' history of fissures. These were associated with a sentinel tag in 39% patients. The fissure healed in 48% of patients, including 75% of patients who previously failed to heal with GTN ointment. There were no recurrences at 3 months and no adverse effects.[23]

No studies were found to compare the effectiveness of diltiazem to commonly used combination cream (proctoheal) in Iraq for the treatment of CAF, but studies were found to compare the effectiveness of DTZ gel or ointment to other combinations like lignocaine and minoxidel.[24] Commonly used over the counter (OTC) combination cream (proctoheal) which is well known for the treatment of anal fissures and haemorrhoids had not been compared to other creams, gel or ointments used for the same purpose, in our study the comparison reveled the superiority of DTZ in both healing and relapse rates, healing of 81% versus 57% of combination cream and relapsing rate of 24% versus 49% of combination cream, with better tolerability by the patients to DTZ gel.

CONCLUSION:

In our study diltiazem 2% gel was more effective than combination cream in the treatment of chronic anal fissure. Other combination creams, ointments and gel had been used commonly by doctors and as OTC treatment of CAF but with less effectiveness.

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