

Efficacy of Diltiazem 2% Cream as a Solid Treatment of Patients with Chronic Anal Fissure at Kirkuk General Hospital

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ABSTRACT

Background: Chronic anal fissure is a common painful benign anorectal case. Surgical operations like lateral internal sphincterotomy or manual anal dilatation are effective for healing most cases within a few weeks. However, as a side effect, permanent impaired anal .continence is likely to occur

Aim: This article aims to evaluate whether the pharmacological can be the first-line option for .the treatment of chronic anal fissure

Patients and Methods: 60 patients are enrolled with a chronic anal fissure in this work. The cases were chosen randomly from Kirkuk general hospital during the period from February 2017 to October 2018. As a first-line therapy, all patients treated with diltiazem 2% cream for .6 weeks

Results: As a result of adverse drug reaction and uncooperative patients, 10 patients were unable to complete medical treatment, while 50 patients were able to complete it.

Furthermore, 40 patients (out of 50) achieved complete recovery with 25 males and 15 females. Nevertheless, 10 patients (7 males and 3 females) were failed to reach complete recovery, which makes undergoing sphincterotomy as a second-line option. Complete recovery is achieved in (n=45) 90% of patients within 5-6 weeks from the start of diltiazem 2% cream. Whereas, 10% of them (n=5) recovered with complete 6 weeks administration of .the cream

Conclusions: For majority patients with a chronic anal fissure, diltiazem 2% cream with a course of six weeks was the first-line choice therapy.

Keywords Chronic Anal Fissure, Diltiazem 2% cream, Medical Sphincterotomy treatment, Lateral Internal Sphincterotomy.

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فعالية كريم الديلتيازيم 2٪ كعلاج متين لمرضى الشق الشرجي المزمن في

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الملخص

خلفية : الشق الشرجي المزمن هو حالة شرجية حميدة مؤلمة شائعة. تعتبر العمليات الجراحية مثل شق العضلة العاصرة الداخلية الجانبية أو توسع الشرج اليدوي فعالة للشفاء في معظم الحالات في غضون أسابيع قليلة. ومع ذلك ، وكنتأثير جانبي من المحتمل أن يحدث ضعف دائم في الشرج .

الهدف : تهدف هذه المقالة إلى تقييم ما إذا كان العلاج الدوائي يمكن أن يكون خيار الخط الأول لعلاج الشق الشرجي المزمن.

المرضى والطرق : تم تسجيل 60 مريضاً مع شق شرجي مزمن في هذا العمل. تم اختيار الحالات بشكل عشوائي من مستشفى كركوك العام خلال الفترة من فبراير 2017 إلى أكتوبر 2018. كعلاج أولي ، تم علاج جميع المرضى باستخدام كريم الديلتيازيم 2 ٪ لمدة 6 أسابيع.

النتائج : نتيجة لرد فعل الدواء الضار والمرضى الغير المتعاونين ، لم يتمكن 10 مرضى من إكمال العلاج الطبي ، في حين تمكن 50 مريضاً من إكماله. علاوة على ذلك ، حقق 40 مريضاً (من أصل 50) الشفاء التام 25 من الذكور و 15 من الإناث. ومع ذلك ، فشل 10 مرضى (7 ذكور و 3 إناث) للوصول إلى الشفاء التام ، مما يجعل الخضوع للعضلة العاصرة كخيار الخط الثاني. يتم تحقيق الشفاء التام في (ن = 45) 90 ٪ من المرضى في غضون 5-6 أسابيع من

بداية استعمال كريم الديلتيازيم 2 % بينما ، 10% منهم (ن = 5) تعافوا مع اكمال المدة الزمنية للعلاج بالكريم والبالغة ستة اسابيع .

الاستنتاجات : بالنسبة لمعظم المرضى الذين يعانون من شق شرجي مزمن ، كان كريم الديلتيازيم 2 % مع دورة من ستة أسابيع علاج الخط الاول للاختبار

الكلمات الدالة: شق شرجي مزمن ، كريم ديلتيازيم 2% ، علاج المصرة الطبية ، شق المصرة الداخلي الجانبي.

1. Introduction

Chronic anal fissure is defined as an ulcer of the anoderm. Distal to the dentate line, typically, it occurs in the midline (whether anterior or posterior) with visible sphincter fibers, anal papillae, sentinel piles and indurated margins [1]. Usually, chronic anal fissure causes severe, sharp anal pain during defecation [2]. About 90% of fissures in male gender are located posteriorly in the midline, while its percentage is equally (i.e., 50% to 50%) in females [3]. Diagnosis can typically be made by physical examination and anoscope if tolerated by the patient [3]. Atypical features, such as multiple, large, irregular fissures, or those not in the midline, may indicate underlying malignancy, sexually transmitted infections, inflammatory bowel disease, or trauma [4]. With more than 6 weeks of symptoms, a chronic fissure is usually deeper and generally has exposed internal sphincter fibers in its base [5]. Based on etiology, it is classified as primary (idiopathic) or secondary. Secondary fissures are those that occur due to some other pathology such as Crohn's disease, anal tuberculosis and patient infected with HIV [4][5]. Chemical sphincterotomy (using calcium channel blockers) is now the first line of treatment globally [6].

Diltiazem cream is very attractive and effective for the treatment of chronic anal fissures. Its mechanism of action is blocking L-type calcium channels in the smooth muscle causing relaxation of the internal sphincter. Consequently, dilate the blood vessels of the anoderm and increase the flow of blood [7]. Topical 2% diltiazem cream supply earlier pain relief with a significant reduction in pain after one week and preceded the significant healing rate of chronic anal fissure [8].

In a study post defecator pain, bleeding and irritation were significantly reduced after two weeks of therapy. Furthermore, a primary healing rate of 86% was achieved at the 6th week of therapy [9]. Although the lateral sphincterotomy remains more effective, it needs to be reserved for cases who fail in responding to chemical sphincterotomy remedy [10].

2. Patients and Methods

This study was applied in Kirkuk General Hospital, Iraq. A total of 60 patients with chronic anal fissure are collected randomly prospectively during the period from February 2017 till October 2018. Symptoms (especially pain) had been present in each patient continuously for at least six months. Full physical examination and digital rectal examination performed for each patient at the time of admission and thereafter. The treatment program consisted of digitally self-application of diltiazem 2% cream two times each day for six weeks as first-line therapy. Meantime, evaluations were carried on patient status regarding pain, bleeding, anal tone and fissure healing in every weekend to observe the patient response to medical treatment. Sphincterotomy was assigned as second-line therapy after failure of medical treatment (A total 6-week course of Diltiazem therapy) or patients' intolerance to medical therapy. Patients with other diseases (hypertension, diabetic and heart disease) were excluded from this study

3. Results and Calculations

As listed in Table 1, the patients were categorized to four ages groups: 1) 20-29 years; 2) 30-39 years; 3) 40-49 years; and 4) ≥ 50 years. Furthermore, the Table presents the number and percentage of males and females. Moreover, Fisher exact indicated 6.6 with p-value 0.0216.

Table 1. The age distributions of patients with a chronic anal fissure for males and females.

Age of patients (year)	Male		Female		Fisher exact	p-value
	N	Percentage (%)	N	Percentage (%)		
20-29	8	6.7	3	2.5	6.6	0.0216
30-39	11	9.2	6	5		
40-49	14	11.7	9	7.5		

≥ 50	5	4.2	4	3.4		
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As mentioned earlier, a total of (38) males and (22) females were involved in this study. As listed in Table 2, fissure locations were: posterior fissure in males (n= 29, 36.65%) and females (n= 3, 6.82%), anterior fissure in males (n= 7, 8.55%) and in females (n= 18, 40.9%), combined (anterior and posterior) in males (n= 2, 3.28%) and in female (n= 1, 2.27%). Pain was present in the all patients with anal fissure while bleeding account for (n= 15, 19.73%) in males and (n=7, 15.90%) in females. (n=19, 24.34%) of males and (n=12, 26.13%) of females patients had sentinel skin tag, (n=6, 7.89%) of males and (n=3, 7.95%) of females had hypertrophied anal papillae, and about (n=3, 4.60%) males ,(n=1, 3.40%) females had combined (sentinel skin tag, hypertrophied anal papillae) or other type (n=10, 13.15% males, n= 6, 12.5% females) of anal fissure.

Table 2. Characteristics of anal fissure for both male and female.

		Male		Female	
		N	Percentage (%)	N	Percentage (%)
Patients(n)		38	100	22	100
Location of fissure	Posterior	29	36.65	3	6.82
	Anterior	7	8.55	18	40.9
	Combined (posterior and anterior)	2	3.28	1	2.27
Symptoms	Pain	38	100	22	100
	Bleeding	15	19.73	7	15.9
Feature of chronicity	1. Sentinel skin tag	19	24.34	12	26.13
	2. Hypertrophied anal papillae	6	7.89	3	7.95
	3. Combination of 1&2	3	4.60	1	3.40
	4. Others	10	13.15	6	12.5

Additionally, about (83%) of patients (n=50) were able to complete the medical treatment, while (17%) of patients (n=10) were unable to complete the medical treatment (see Figure 1).

As demonstrated in Figure 2, the major causes for stopping the medical treatment was because of headache 40%, flushing 35%, hypotension 10%, and tachycardia 10%.

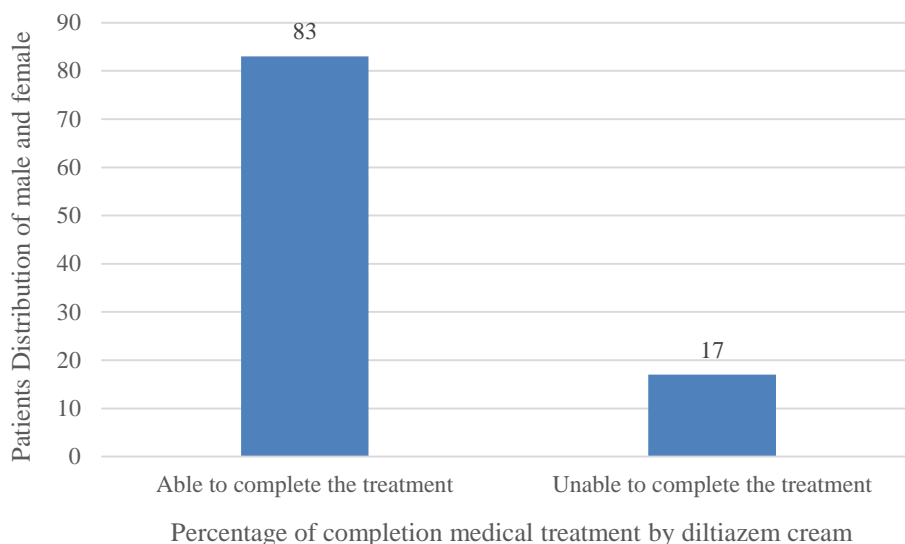


Figure 1. Patients Distribution % according to completion of medical treatment by diltiazem 2% cream.

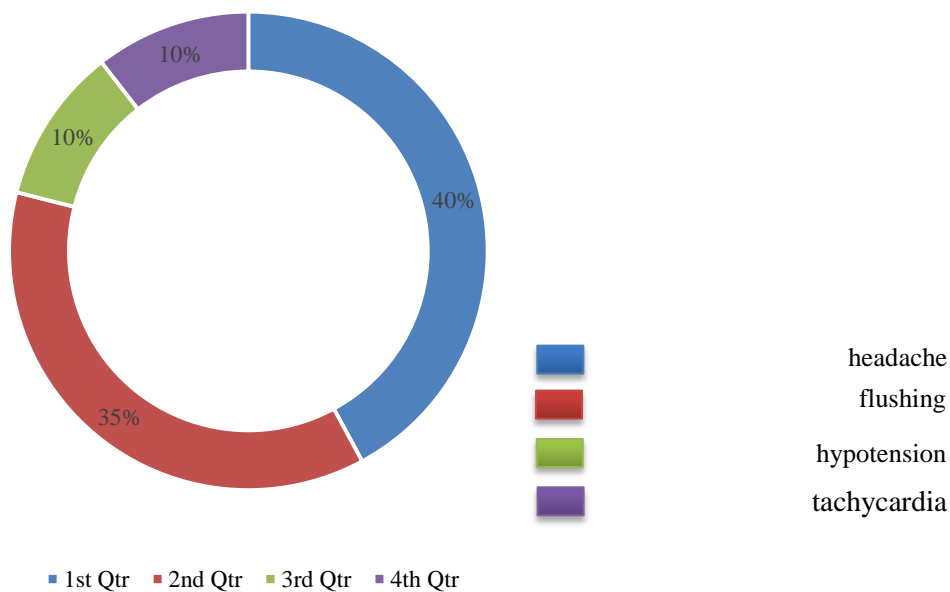


Figure 2. Patient Distribution according to cessation the treatment by diltiazem 2% cream

The cases showed that there was a significant relationship between patients' response to diltiazem cream therapy and the degree of anal fissure chronicity (especially Sentinel Skin Tag); were p -value= 0.0005 (see Table 3).

Table 3. Patient distribution according to respond to medical treatment by diltiazem cream and degree of anal fissure chronicity.

Feature of chronicity	Response to treatment by diltiazem cream		Failure of response to treatment by diltiazem cream		Fisher exact	p-value
	N	Percentage (%)	N	Percentage (%)		
1. sentinel skin tag.	22	44	4	8	57	0.0005
2. hypertrophied anal papillae.	6	12	2	4		
3. combination of 1&2.	2	4	2	4		
4. others	1	2	11	22		

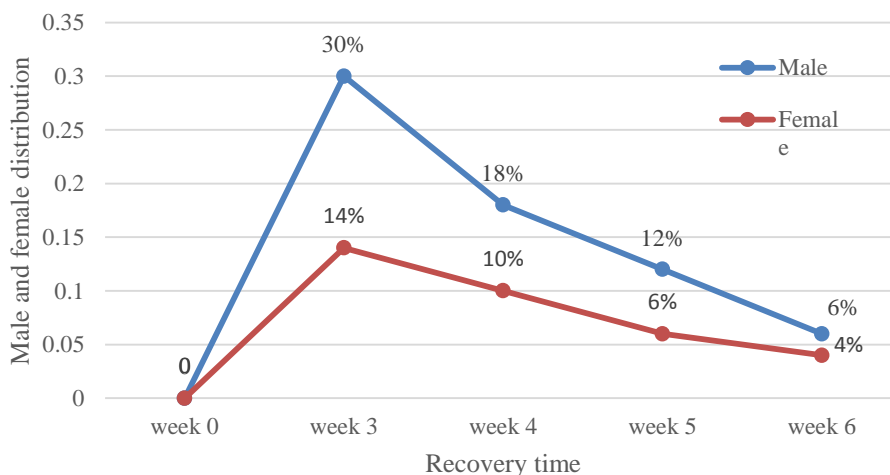


Figure 3. (male and female) distribution according to recovery time

4. Conclusion

In this article, we evaluated whether the pharmacological can be the first-line option for the treatment of chronic anal fissure. The findings showed that most of the patients were middle-aged. Digital application of topical diltiazem 2% cream is first-line therapy for chronic anal fissure and the best drug of choice for patients with best response rate, within 6 weeks treatment course.

5. Statistical Analysis

All patients' data are entered using computerized statistical software SPSS (version 17) was implemented. We used Fisher's exact test for categorical variables.

6. Discussion

This study is present that higher degree incidence of chronic anal fissure between Age 40-49 years (19%), then age 30-39years (14%), followed by age 20-29 years (9%). Besides, only (7%) were at age ≥ 50 -year-old which is no congruent with study done by (Douglas W Mapel, Michael Schum, and Ann Von Worley) and the study that done by (Abro AH, Agha AH, Laghari AR, Bhurgari A, Ali S and Ali SA) in 2014 and 2015, respectively [11] [12]. Incidence of fissure was more common in male (31.8%) than in female (18.4%) that not agree with study done in 2015 about Chronic Anal Fissure – A Multi Centric Study [12]. However, it agrees with study to assess the effectiveness and side effect of diltiazem 2% gel in the management of chronic fissure-in-ano in 2015 [13]. Furthermore, 83% of patients were able to complete the medical treatment and only 17% discontinued the medication due to side effect of drug and underwent surgery as second-line therapy. This finding disagrees with study done in 2012 by Majid Aziz, Faran Kiani and Shahzad Ahmed Qasmi [14], but agrees with other study done in 2014 [15].

The most common adverse effect of the drug was headache 40% and flushing 35% which donot agree with another work in [15]. The rate of fissure healing in group of patients who are responded to medical treatment by diltiazem to other groups who fail to treatment was (62% versus 38%). There was a significant relationship between patients' response to diltiazem 2% cream therapy and the degree of anal fissure chronicity (especially Sentinel Skin Tag) that was is agree with Comparative Study of Lateral Sphincterotomy and 2% diltiazem gel local application in the treatment of chronic fissure applied in 2014 [16]. In the course of total 6-week treatment by diltiazem 2% cream, 30% of males and 14% of females achieved recovery

within 3 weeks. Additionally, 18% of male and 10% of female recover within 4 weeks, 12% of male and 6 % of female recover within five weeks, and 6% of male, 4% of female recovered with 6 weeks. This outcome is congruent with study accomplished by Rajan Vaithianathan and Senthil Panneerselvam (Randomised Prospective Controlled Trial of Topical 2% Diltiazem Versus Lateral Internal Sphincterotomy for the Treatment of Chronic Fissure) in 2015 [17].

Finally, no patient achieved recovery in the first two weeks of establishing treatment which was agreed with another study in 2013 [18].

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