Botulinum toxin versus surgical sphincterotomy in females with chronic anal fissure

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ABSTRACT

الأهداف: للمقارنة بين استخدام البوتوكس (BTX)، والعملية الجراحية في التئام الشرخ الشرجي المزمن (CAF) أو ارتداده.

الطريقة: أجريت هذه دراسة في مستشفى الملك عبد العزيز الجامعي – جدة –المملكة العربية السعودية، على مدى ثلاث أعوام خلال الفترة ما بين يناير 2004م وحتى ديسمبر 2006م. تم فيها المقارنة بين (100) سيدة مصابة بمرض الشرخ الشرجي المزمن (CAF) وذلك باستخدام الجراحة لـ(50) مريضة في المجموعة الأولى، وباستخدام البوتوكس (BTX) لـ(50) مريضة في المجموعة الثانية.

النتائج: بعد استيفاء الدراسة تبين أن العلاج الجراحي أدى إلى شفاء تام لدى جميع مريضات المجموعة الأولى بنسبة (100%)، ولم تحدث أية حالة ارتداد للشرخ خلال الثلاث سنوات، إلا أن حالة واحدة أُصيبت بعدم قدرة على التحكم بمقبض الشرج بشكل جزئي دائم. أما مريضات المجموعة الثانية والآتي تم علاجهن باستخدام البوتوكس فقد وصلت نسبة الشفاء لديهن إلى (86%) (p=0.006). عشرة منهن فقدن القدرة على التحكم بمقبض الشرج بشكل جزئي ومؤقت (p=0.014)، وسبعة مريضات أُصبن بانتكاسة بعد ستة اشهر (14%) (p=0.006).

خاتمة: أكدت هذه الدراسة إن استخدام البوتوكس (BTX) كعلاج أولي قبل الجراحة يعتبر آمن لعينة مختارة من المريضات اللاتي يعانين من الشرخ الشرجي المزمن (CAF).

Objectives: To compare the effectiveness and the morbidity of botulinum toxin (BTX) in the treatment of chronic anal fissure (CAF) versus the standard surgical sphincterotomy.

Method: One hundred female patients with CAF were treated by either closed lateral sphincterotomy [surgical group (Group I, n=50 patients)] or BTX 40 IU [chemical group (Group II, n=50 patients)]. The study was conducted in the King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia, over 3 years between January 2004 and December 2006.

Results: The healing rate was 100% in surgical group with no recurrence on the period of 3 years follow up and one patient has partial permanent incontinence. While in chemical group the healing rate was 86% (p=0.006). Ten patients had transient incontinence (p= 0.014). Seven patients had recurrence within 6 months 14% (p=0.006).

Conclusion: We conclude that chemical sphincterotomy is safe, effective first line treatment in selected female patients with CAF.

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Anal fissure continues to be the most common anal problem manifested by intense anal pain, and fresh bleeding on defecation.[1,2] Chronic anal fissures (CAF) are associated with persistent hypertonia of the internal anal sphincter with manometric evidence of internal sphincter spasm.[3,4] Over the last century, variety of surgical procedures have been described in order to relieve the spasm, and to decrease elevated resting pressure, thereby allowing the fissure to heal, and lateral sphincterotomy has become the procedure of choice with rate of recurrence smaller than 10%.[5-8] However, the high rate of incontinence as much as 66% reported in surgical sphincterotomy[9] has led to implementation of other alternative medical treatments mainly botulinum toxin (BTX),[10-13] and organic nitrate preparations,[14,15] which led to reduction of anal sphincter pressure,

allowing healing of the fissure. Botulinum toxin comprise a family of neurotoxins designated as types A-G, which are produced by the anerobic bacterium *Clostridium* botulinum. Botulinum toxin-A blocks cholinergic transmission leading to flaccid paralysis, and autonomous nerve dysfunction. Chronic anal fissures are caused by anal sphincter hypertonia leading to an ischemic ulcer. Botulinum toxin injection into the internal, or external anal sphincter causes relaxation of the anal sphincters, enhances microcirculation at the fissure site, and promotes fissure healing.[16] Thus, the aim of this prospective study is to compare morbidity, and the effectiveness of surgical closed lateral sphincterotomy under general anesthesia as day care procedure, and BTX toxin injection on out patient clinic under no anesthesia in the treatment of anal fissure in females.

Methods. One hundred consecutive female patients with CAF were assigned to surgical sphincterotomy (Group I, n=50), or chemical sphincterotomy with BTX 40 IU (Group II, n=50). The study was conducted in the King Abdul-Aziz University Hospital, Jeddah, Kingdom of Saudi Arabia between January 2004 and December 2006. Medical ethics committee approval was taken before the study was started, and we obtained all patients consent during the study period. All patients were females and diagnosed clinically as CAF based on their history and physical examination. Conservative treatment with local creams, suppositories, and warm sitz baths were tried before inclusion in the study. The CAF was defined as the presence of fissure in ano? with exposed internal anal sphincter. The exclusion criteria were associated anal pathologies as second or third degree internal hemorrhoids, perianal fistula or abscess, anticoagulants therapy, and pregnancy. In the surgical group, the sphincterotomy was carried out as a day surgery under general anesthesia. The sphincterotomy was performed by one surgeon, and the closed technique procedure was carried out. The sphincterotomy was performed, while the patient on lithotomy position using blade 11 at 9 o'clock position. The intersphincteric space was identified where the knife was placed, and the index finger of the other hand placed inside the anus to control the knife. The lower part of the internal sphincter was cut without opening the anal mucosa then pressure dressing was applied. The patient was discharged on the same day. The chemical sphincterotomy was carried out using the 100-IU vials of type A BTX (Botox, Allergan, Inc, Trvine, CA, USA), which was stored at temperature of 20^{0}C, and diluted in one ml of normal saline, the dilution was carried out immediately before the injection. The injection was carried out at outpatient clinic using a 25 gage needle without anesthesia, and 0.4 ml of diluted toxin injected, and 0.2 ml in each side of the fissure. The injection was applied into the internal sphincter by feeling the sphincter. On both groups, patients were put on high fiber diet, worm sitz baths, laxatives, and analgesic. Patients were followed up for the degree of pain, bleeding, constipation, healing, incontinence, after one week, 4 weeks, and after 6 months, 3 years after for recurrence and incontinence. Healing was defined by the disappearance of the fissure regardless of symptoms. Generally, there were no significant differences between the 2 groups about the characteristics of the patients, and/or the clinical examination at the start of treatment (**Table 1**).

Statistical Analysis. The data were managed and analyzed using SPSS version 15.0. The descriptive data were managed by mean ± standard deviation (mean±SD). We compare the age and the severity of pain of both goups using the students t-test. Pearson Chi-Square was used to compare the 2 groups in many parameters such as bleeding, healing, constipation, incontinence, and recurrence. The difference of the 2 groups were statistically significant (p<0.05).

Results. One hundred female patients were included. Fifty patients underwent closed lateral sphincterotomy (Group I), and 50 received BTX toxin (Group II). Both groups were identical, patient's age were range between 18-62 years (mean 33.10). The clinical presentations of both groups were similar, and pain was the most common presentation and it was the presenting symptom of all the patients in both groups. The severity of the pain was analyzed using the visual analog score. The pain severity

Table 1 - Demographic data and characteristics of female patients.

Characteristics	Group I (n=50) (closed lateral sphincterotomy)	Group II (n=50) (Botulinum injection)	*P*-value
Gender:	50	50	
Mean age (years)	34.30 ± 9.9	31.90 ± 12.4	0.287
Pain severity (VAS)	8.0 ± 1.2	7.8 ± 1.4	0.399
Pain duration >2 years	18 (36)	15 (30)	0.523
Bleeding	22 (44)	19 (38)	0.542
Bleeding duration >2 years	1 (4.8)	2 (10)	0.520
Constipation	46 (95)	40 (80)	0.017
Constipation duration (years)	19 (38)	16 (32)	0.529
Anal itching	3 (6)	1 (2)	0.0307
Site of fissure			
Posterior midline	44 (88)	42 (84)	0.564
Anterior midline	5 (10)	71 (4)	0.538
Multiple fissures	1 (2)	1 (2)	1.000

VAS - visual analog score

Table 2 - Complications and results of treatment.

Complications	Group I (n=50) surgical	Group II (n=50) chemical	*P*-value
	(n= %)		
Hematoma	0 (0)	1 (2)	0.315
Perianal fistula	1 (2)	0 (0)	0.315
Perianal abscess	0 (0)	1 (2)	0.315
Healing	50 (0)	43 (86)	0.006
Incontinence after one week	1 (2)	10 (20)	0.014
Incontinence up to 3 years	1 (2)	0 (0)	0.315

BTX - botulinum toxin

and the pain duration were similar in the 2 groups. The constipation was the presenting symptom in most of the patients in both groups. Bleeding was present in 22 of the patients in Group I, and 19 of the patients in Group II. Patient's demographic data for both groups are summarized in **Table I**. Healing occurred in all the patients who underwent lateral sphincterotomy, while 43 patients (86%) had healing in BTX group. Transient incontinence occurred in 10 patients in BTX group that lasted between 7-10 days, while prolonged incontinence occurred in one patient from the surgical sphincterotomy. There was no recurrence in the surgical group, while it occurred in 7 patients in BTX group all of which occurred within the first year. The recurrence was treated conservatively except for one patient treated with surgical sphincterotomy. Result of treatment and complications in both groups are summarized in **Table 2**.

Discussion. Chronic anal fissure is a common health problem affecting both gender. In cases resistant to conservative treatment, surgical sphincterotomy is the standard treatment. This procedure associated with devastating complication, which is the faecal incontinence up to 66%[8,9] especially in high-risk group such as females. Non-surgical treatment modalities have been developed. Many studies addressed the use of chemical agents mainly the BTX toxin and organic nitrate preparations[10-15] to relieve sphincter spasm with medical sphincterotomy, which reduce the internal sphincter spasm allowing the healing of the fissure. Smooth muscle relaxation is an effective treatment for CAF, and has advantages over surgical treatment in avoiding long-term complications, additionally, it does not require hospitalization. The pharmacological agent that effectively causes temporary sphincterotomy, and heals most fissures has led to approximately two-thirds of patients avoiding surgery.[15] Smooth muscle relaxation is also the first option in patients with a high risk of incontinence.[16] Studies of BTX injection into the anal sphincter have reported excellent healing rates between 73-87% with direct relation between the rate of healing and the dose of BTX.[17, 18] The healing rate was 73% when 20U was used and 87% with dose of 30-80U (p=0.04). Some patients in the high dose group developed mild incontinence of flatus that lasted 2 weeks after the treatment and disappeared spontaneously.

In this study, we randomized 100 female patients to either surgical sphincterotomy, or to BTX toxin injection over the period of 3 years. The healing rate was higher in the surgical group, and it was statistically significant (p=0.006). The long term incontinence occurred in one patient from the surgical group, which lasted up to 3 years. It was treated conservatively by sphincter exercise and the patient had a symptomatic improvement to the incontinent, while in the chemical group none of the patients had long term incontinence. One patient developed perianal fistula at the site of sphincterotomy treated with surgical excision. Recurrence occurred in 14% of the chemical group, while none of the patients in the surgical group had recurrence over the period of follow-up. Out of the 7 patients of the recurrence group, 5 patients responded to the conservative treatment, while the remaining 2 patients, were treated by surgery, and alternative treatment using the traditional medicine. We found that the results of our study is similar to other studies, but no similar rate of recurrence and this could be due to the control of constipation which was the precipitating cause of fissure in most of our patients. It was present in 46 (95%) in the surgical group and 40 patients (80%) in the chemical group, while it was present in 10 present in all the patients in the first 4 weeks post treatment by either surgical sphincterotomy, or by BTX injection.

In conclusion, CAF is a common anal problem, and BTX toxin is a safe effective mode of treatment and it should be used as first line treatment in selected female patients who failed the conservative treatment.

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