



Surgical versus chemical (botulinum toxin) sphincterotomy for chronic anal fissure: long-term results of a prospective randomized clinical and manometric study

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Abstract

Background: The aim of this prospective randomized trial was to compare the effectiveness and morbidity of surgical versus chemical sphincterotomy in the treatment of chronic anal fissure after a 3-year follow-up.

Methods: Eighty patients with chronic anal fissure were treated by whether open lateral internal sphincterotomy (group 1) or chemical sphincterotomy with 25 U botulinum toxin injected into the internal sphincter (group 2). Clinical and manometric results were analyzed.

Results: Overall healing was 92.5% in the open sphincterotomy group and 45% in the toxin botulinum group ($P < .001$). There is a group of patients with clinical (duration of disease >12 months and presence of a sentinel pile before treatment) and manometric factors (persistently elevated mean resting pressure, % of time presence of slow waves, and number of patients or the time presence ultra slow waves after treatment) associated with a higher recurrence of anal fissure. The final percentage of incontinence was 5% in the open sphincterotomy group and 0% in the botulinum toxin group ($P > .05$).

Conclusion: We recommend surgical sphincterotomy as the first therapeutic approach in patients with clinical and manometric factors of recurrence. We prefer the use of botulinum toxin in patients older than 50 years or with risk factors for incontinence, despite the higher rate of recurrence, since it avoids the greater risk of incontinence in the surgical group. © 2005 Excerpta Medica Inc. All rights reserved.

Keywords: Anal fissure; Sphincterotomy; Botulinum toxin

Anal fissure remains one of the most common proctologic problems manifesting as pain and bleeding on defecation [1,2]. Chronic anal fissures are associated with persistent hypertonia of the internal anal sphincter, and manometric evidence of internal sphincter spasm reflecting elevated resting anal pressures has been reported [3,4].

Over the last century, a variety of surgical methods [5] have been described in order to eliminate this spasm and decrease the elevated anal pressures, thereby allowing the fissure to heal. The objective of all these methods is to obtain a high rate of healing associated with a low rate of morbi-mortality, and lateral internal sphincterotomy has become the procedure of choice with rates of recurrence smaller than 10% [6–8].

However, the high rates of incontinence, as much as 66% reported in the case of surgical sphincterotomy [9], have led

to the study and implementation of other alternative medical treatments, mainly botulinum toxin [10–15] and organic nitrate preparations [15–17], that produce reversible reduction in sphincter pressure, allowing the healing of the anal fissure. Of these, botulinum toxin has achieved the lowest rates of recurrence [12] with the fewest side effects [18] when compared with the results described in the case of nitrate preparations.

Thus, the aim of this prospective randomized controlled trial was to compare the effectiveness and morbidity of surgical (ambulatory open lateral internal sphincterotomy realized with local anesthesia) and chemical (botulinum toxin) sphincterotomy in the treatment of chronic anal fissure.

Methods

Between January 1998 and January 2000, 80 consecutive patients with chronic anal fissure were assigned according

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to a computer randomization program to surgical sphincterotomy (group 1, $n = 40$) or chemical sphincterotomy with botulinum toxin (group 2, $n = 40$). This study (first visit, sphincterotomy, and postoperative revision) was done in an ambulatory setting in the Coloproctology Unit of Elche University Hospital. The study was approved by the Ethics Committee and each patient signed the informed consent before participating in the study.

First, all patients were diagnosed as having chronic anal fissure based on their medical history and physical exploration, and treated for a minimum of 6 weeks with conservative medical treatment (high residue diet, analgesics, and warm sitz baths) before definitive definition of chronic anal fissure and inclusion in the study. Chronic anal fissure was defined as the presence of a fibrous induration or exposed internal sphincter fibres.

The exclusion criteria were associated anal pathologies (any degree of stenosis due to anatomic alteration regardless of an hypertonic anal sphincter, abscess, fistula, and any degree of symptomatic hemorrhoids), associated conditions (inflammatory bowel disease, acquired immunodeficiency syndrome, tuberculosis, sexually transmitted disease, and immunosuppression), anticoagulative therapy, allergy to local anesthetics, and pregnancy.

All patients were treated by the same surgeon using a uniform method in the prone jackknife position. All patients had a pulse oxymeter monitor and did not need preoperative laboratory tests, enema preparation, antibiotics, or intravenous access.

In the surgical sphincterotomy, the open lateral internal sphincterotomy was performed under local anesthesia (20 mL mepivacaine 2%) using a 25-G needle. The anesthetic was injected into the skin, intersphincteric plane, internal sphincter, and submucosa on the right and left side. The fissure furrow was also infiltrated. The open technique was performed by exposing the right lateral anal region with an anal retractor, and a 1- to 2-cm skin incision was made in the intersphincteric groove. The anal mucosa was separated from the internal sphincter all the way down to the dentate line. The intersphincteric plane was entered and the sphincters separated. The distal internal sphincter was incised under direct vision using electrocoagulation. The skin incision was not closed and direct pressure was applied for 5 minutes.

In the chemical sphincterotomy group, the 100-U vials of type A lyophilized botulinum (BOTOX, Allergan, Inc, Irvine, CA) were stored at a temperature of -20°C and diluted in saline to 0.1 mL/2.5 U on the day of injection. With a 25-G needle, a total of 25 U was injected into the internal sphincter guided under direct vision and digital examination (8-U dose into each lateral side of the sphincter and 9 U into the anterior verge).

In both groups, the patients were discharged with instructions concerning high residue diet, analgesics (oral met-anizol 1 capsule [575 mg] every 8 hours alternating with oral ketorolac 1 capsule [10 mg] every 8 hours), and warm

sitz baths. Early complications were collected at 1 week revision. Information regarding sex, age, symptoms, bowel habits, examination findings, manometric values, fissure healing, and recurrence was collected at the time of admission and at 2-month, 6-month, 1-, 2-, and 3-year follow-up visits. Follow-up evaluation was performed by other different surgeon attached to the Coloproctology Unit. Healing was defined as complete re-epithelization of the fissure and absence of symptoms. Recurrence of fissure was defined by persistence of fissure in anatomic exploration whether associated with symptoms or not. The Cleveland Clinic Scoring System was used for assessment of incontinence [19].

Anorectal manometry was performed using a low-compliance water perfusion system with a filled 6-lumen catheter (external diameter, 4 mm) having radially arranged ports in cross-section. Pressures were recorded by means of a pressure situated within each infusion line and connected to a recording chart. With the patient in the left lateral position with flexed knees and hips, the probe was introduced 6 cm into the anal canal then withdrawn at 1-cm intervals and ultra slow waves, slow waves, mean squeeze pressure, and mean resting pressure in mm Hg were recorded. The results were compared with the normal range for our laboratory in 100 healthy patients (control group): mean resting pressure = 66 ± 23 mm Hg and mean squeeze pressure = 164 ± 60 mm Hg (control group).

Generally, there were not significant difference between the 2 groups in the characteristics of patients, symptoms, and anal exploration before treatment (Table 1).

Statistical analysis

The data were analyzed by standard statistical methods and the results expressed as means \pm SD. Differences between manometric data were compared using Student *t* test for paired and unpaired samples, whereas differences between percentages were analyzed using Fisher exact test. Probability values of less than .05 were considered significant. Analysis of variance was used to compare variables between the groups.

Results

Complications and results of treatment are listed in Table 2. We found 2 patients (5%) with an hematoma wound (1 in the surgical sphincterotomy group and 1 in the chemical sphincterotomy group) and only 1 patient with a self-limited bleeding wound in the surgical sphincterotomy group. There were no anal abscesses, hemorrhoid thromboses, perianal fistulae, or urinary retention.

There was persistence or recurrence of the fissure in 1 patient (2.5%) in the surgical sphincterotomy group and in 6 patients (15%) in the chemical sphincterotomy group ($P > .05$) at the 2-month visit, and 1 more patient in the surgical sphincterotomy group (overall, 5%) and 6 more

Table 1
Characteristics of patients, symptoms, and anal exploration before treatment

	Group 1 (n = 40) open sphincterotomy	Group 2 (n = 40) toxin botulinum	P
Mean age (y)	38 ± 14	41 ± 15	
Gender (men/women)	29 (72.5%)/11 (27.5%)	26 (65%)/14 (35%)	
Symptoms duration (mo)	20 ± 21	18 ± 18	
Site of fissure			
Posterior midline	30 (75%)	32 (75%)	>.05
Anterior midline	10 (25%)	10 (25%)	
Skin tag	28 (70%)	30 (75%)	
Pain	36 (90%)	37 (92.5%)	
Bleeding	34 (85%)	33 (82.5%)	
Constipation	28 (70%)	27 (67.5%)	
Pruritus	20 (50%)	23 (57.5%)	
Anal hypertonia			
Slight	4 (10%)	5 (12.5%)	
Moderate	26 (65%)	20 (50%)	
Inexplorable	10 (25%)	15 (37.5%)	

patients in the chemical sphincterotomy group (overall, 30%) ($P < .05$) after 6 months. Differences in overall healing were found during the 1-year review: 37 patients (92.5%) in the surgical sphincterotomy and 18 patients (45%) in the chemical sphincterotomy group ($P < .001$). There were no new recurrences at the 2- and 3-year follow-up evaluations.

Fissures were significantly less likely to heal in patients in whom the condition had been present for longer than 12 months and who had a sentinel pile. No relationship was found between the other preoperative clinical variables analyzed and healing.

The mean preadmission and post-treatment resting and squeeze manometric pressures are shown in Table 3. The range of preoperative mean resting pressure in both groups was similar, with medians of 109 ± 29 mm Hg (range

Table 2
Complications and results of treatment in the two groups

Complications (n = %)	Group 1 (n = 40) open sphincterotomy	Group 2 (n = 40) toxin botulinum	P
Hematoma	1 (2.5%)	1 (2.5%)	>.05
Hemorrhage	1 (2.5%)	0 (0%)	
Anal abscess or fistula	0 (0%)	0 (0%)	
Hemorrhoid thrombosis	0 (0%)	0 (0%)	
Incontinence			
2-month	3 (7.5%)	2 (5%)	
6-month	2 (5%)	0 (0%)	
1-2-3-year	2 (5%)	0 (0%)	
Recurrence			
2-month	1 (2.5%)	6 (15%)	>.05
6-month	1 (2.5%)	6 (15%)	
1-year	1 (2.5%)	10 (25%)	<.05
2-year	0 (0%)	0 (0%)	
3-year	0 (0%)	0 (0%)	
Overall	3 (7.5%)	22 (55%)	<.001

59.8–157.7) in patients with surgical sphincterotomy, and 114 ± 25.7 mm Hg (range 60–164) in the chemical sphincterotomy group ($P > .05$). Raised mean resting pressure was found in patients with anal fissure before treatment as compared with the control group ($P < .001$), whereas no significant difference was found between the mean squeeze pressure in the 2 groups. After treatment, the mean resting pressure decreased significantly ($P < .001$) in both groups as compared with previous pressures. The percentage of reductions in mean resting pressure was greater in the surgical sphincterotomy group (32.7%) than in the chemical sphincterotomy group (19.7%), and this was directly associated with a greater percentage of overall healing in the surgical sphincterotomy group.

The differences between the mean resting pressure and the mean squeeze pressure in patients with healing and in those with no healing or recurrent fissure at consecutive reviews over time can be seen in Fig. 1. The mean resting pressure in patients with healing at 3 years was 75.65 mm Hg, whereas it was 112.85 mm Hg in patients with recurrent fissure ($P < .001$) who had similar values to those prior to treatment. There were not significant differences in the mean squeeze pressure.

Table 3
Mean preadmission and post-treatment resting and squeeze manometric pressures as a function of the type of treatment

	Group 1		Group 2	
	MRP	MSP	MRP	MSP
Preoperative	109 ± 29	200 ± 79.5	113.9 ± 25.7	193 ± 68
2-month	72.5 ± 20.3	178.6 ± 73.4	85.9 ± 22.4	173.6 ± 62.4
6-month	72 ± 9.2	185.7 ± 68.3	88.7 ± 24.5	197.8 ± 61.2
1-year	73.4 ± 17.1	188.2 ± 62	91 ± 26	188.5 ± 47.8
2-year	70.2 ± 19.3	183.9 ± 70	92.1 ± 15	190.5 ± 30
3-year	72.4 ± 17	187.2 ± 60	91.5 ± 26.3	187.5 ± 47

Data are presented in mm Hg. Values are means ± SD. MRP = mean resting pressure; MSP = mean squeeze pressure.

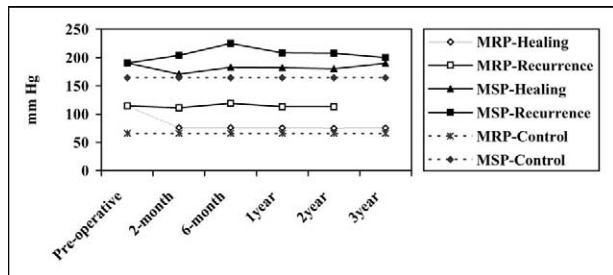


Fig. 1. Mean resting pressure (MRP) and mean squeeze pressure (MSP) in healing or recurrence fissure.

Slow waves were present in 96 patients (96%) of the control group and in 76 patients (95%) with anal fissure before treatment. Slow waves were present for longer periods of time (90%) in patients with fissure than in controls (65% of time) ($P < .01$). Successful treatment reduced the percentage of time presence of slow waves to normal levels, but did not significantly modify the number of total patients with slow waves (72 patients). There were no significant differences between the surgical sphincterotomy and chemical sphincterotomy groups.

Ultra slow waves were recorded in 64 patients (80%) in the fissure group before treatment and in 25 patients (25%) of the control group ($P < .01$). Ultra slow waves were present in patients with fissure before treatment for longer periods of time than in controls (70% vs 10%, $P < .001$). Contrary to patients with recurrence of the fissure, whose ultra slow wave values remained unchanged as before treatment, in healed patients the number with ultra slow waves was reduced significantly to 16 patients (20%) and the percentage of time (20%) that the ultra slow wave was present decreased to values similar to those found in the control group. There were not significant differences between the surgical sphincterotomy and chemical sphincterotomy group.

With regard to incontinence, in the 2-month revision it was present in 3 patients (7.5%) in the surgical sphincterotomy group and in 2 patients (5%) in the chemical sphincterotomy group. Of the patients who reported incontinence, 2 patients in surgical sphincterotomy group and 1 patient in chemical sphincterotomy group had occasional incontinence for liquid feces, while the remaining patients were only occasionally incontinent to flatus. At the 6-month revision, all patients in the chemical sphincterotomy group and 1 patient in the surgical sphincterotomy group reported that incontinence had spontaneously resolved. After 1 year, only 2 patients from the surgical sphincterotomy group (5%) reported occasional residual incontinence to flatus (<4, Cleveland score). At the revisions after 2 and 3 years, no changes in incontinence were found. These differences between the 2 groups in the percentages of incontinence with regard to the treatment used were not significant.

Fig. 2 shows the evolution of the mean resting pressure and mean squeeze pressure with time in the group of incontinent patients as compared with the continent patients. A

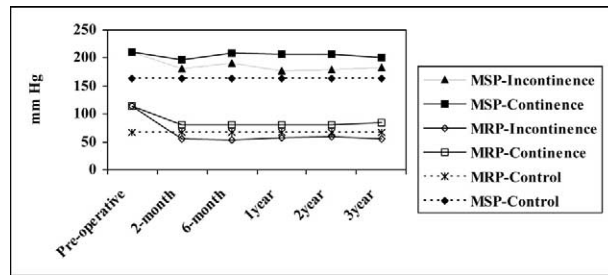


Fig. 2. Mean resting pressure (MRP) and mean squeeze pressure (MSP) in incontinent and continent patients.

statistically significant difference was found in the manometric values at the 2-month revision between the mean resting pressure (55.1 ± 7.9 mm Hg) in incontinent patients and the mean resting pressure (80.7 ± 21 mm Hg) in continent patients ($P < .001$), whereas the difference between the mean squeeze pressure (180.9 ± 56.7 mm Hg) in incontinent patients and the mean squeeze pressure (196.7 ± 68.4 mm Hg) in continent patients was not significant. Of all the preoperative clinical variables analyzed, only age greater than 50 years was associated with incontinence. All the incontinent patients were older than 50 years of age.

Comments

There is still controversy on whether botulinum toxin is bound to replace surgical sphincterotomy as the treatment of choice for chronic anal fissure. Many studies have been published about treatment with botulinum toxin [10–14] or surgical sphincterotomy [5–8]; however, only Mentis et al [20] reported a prospective randomized study comparing them, with a short (12 months) clinical follow-up. Our study is the first prospective randomized study with a long-term (36 months) clinical and manometric follow-up.

If we analyze the studies with longer follow-up times [20,21], it is possible to see in botulinum toxin treatments a trend to progressive recurrence over time with lower healing rates than those initially reported. Minguez et al [22] present the longest-term follow-up (42 months) with a relapse of anal fissure in 41.5% of patients. Our study also shows this tendency only in botulinum toxin group, since there is a progressive rate of recurrence, which starts at 12% in the early months and reaches 53% at 3 years. In surgical sphincterotomy, the recurrence is lower (<10%) and not progressive. This is not surprising, since it could be related to the temporary reversible effect of the toxin contrary to the surgical sphincterotomy. In addition, it can be seen that recurrence occurs mainly between 6 and 12 months, so later relapses are not expected.

Some studies describe clinical factors related to recurrence [22,23]; in our study we can also find some clinical parameters related to a higher rate of recurrence indicating that the fissure has become chronic (duration of disease over

12 months and presence of a sentinel pile), and therefore reversible sphincterotomy with botulinum toxin does not appear to be sufficient to achieve definitive healing.

When we analyze the manometric data recorded, we can see that patients with anal fissure present elevated resting anal pressures before treatment. Recurrence was closely related to persistence of the fissure spasm or its manometric equivalent of persistently high mean resting pressure, a basic etiopathogenic mechanism of fissures [3,4]. These differences were also seen when comparing the type of treatment used, since in the surgical sphincterotomy group this reduction in the mean resting pressure was almost double that of the botulinum toxin group (32.7% vs 19.7%), and this fact is directly associated with a higher rate of recurrence in the chemical sphincterotomy group.

Prior manometric studies in patients treated with surgical sphincterotomy found important pathophysiologic implications of marked fluctuations of anal canal resting pressure, known as slow and ultraslow waves [3,24,25]. However, these manometric variables have not been analyzed previously in patients treated with botulinum toxin.

Slow waves are low amplitude oscillations about baseline resting pressure, which represent the basal electrical activity of the internal anal sphincter. In our study, we found no difference in the total number of patients with slow waves between the control group and the group with anal fissure (96% vs 95%); however, slow waves were present for longer periods in fissure patients (90% of time) as compared to controls (65% of time). Successful treatment reduced this % of time presence of slow waves to normal levels, but did not significantly modify the total number of patients with slow waves [3,25].

In contrast, ultra slow waves are high amplitude pressure variations, generated by a hypertensive irritable internal anal sphincter that occur in conjunction with a raised anal resting tone [3,25]. They are associated with the presence of hemorrhoids, anal fissures, proctalgia fugax, and constipation; they are rarely observed in healthy persons. In our study we found ultra slow waves in 80% of patients in the fissure group and in 25% of patients in the control group. Moreover, ultra slow waves were present in patients with fissure for longer periods than in controls (70% vs 10% of time). Successful treatment significantly reduced the number of patients and the time presence of ultra slow waves to the normal values found in the control group, and led to an improvement in the symptoms.

In conclusion, there is a group of patients with clinical (duration of disease >12 months and presence of a sentinel pile before treatment) and manometric factors (persistently elevated mean resting pressure, percentage of time presence of slow waves, and number of patients or the time presence ultra slow waves after treatment) associated with a higher recurrence of anal fissure. Therefore, we believe that in these patients surgical treatment should be considered as the first therapeutic option in the view of the high probability of

recurrence with botulinum toxin treatment in the long-term follow-up.

On the other hand, we found no significant difference between the 2 groups in the immediate complication rates (hemorrhage, hematoma wound, retention of urine, etc) following treatment. The rate of permanent incontinence after three years was 5% in the surgical sphincterotomy and 0% in the botulinum toxin group, which is associated to a lower mean resting pressure and mean squeeze pressure than in continent patients. An age of greater than 50 years was the only pretreatment factor associated with an increase in incontinence. Concerning the morbidity of botulinum toxin [18], the bibliography points out its safety on the grounds of the infrequent complications that arise (incontinence, postinjection hemorrhoidal thrombosis, anal hematoma, and epididymitis) and their banal and reversible nature. In our series, only 5% reported initial incontinence, which was 100% reversible and progressively disappeared as the internal sphincter recovered its functionality. Based on these findings, we recommend the use of botulinum toxin as the first therapeutic approach in patients older than 50 years or with risk factors for incontinence (women who have had multiple vaginal deliveries, prior anal surgery, prior incontinence, inflammatory bowel disease, etc), despite the higher rate of recurrence associated with this treatment, since it avoids the greater risk of incontinence found in the surgical group.

References

- [1] Oh C, Divino CM, Steinhagen RM. Anal fissure. 20-year experience. *Dis Colon Rectum* 1995;38:378–82.
- [2] Rohde H. The pathogenetic mechanism causing anal fissure. *Int J Colorectal Dis* 2003;18:95.
- [3] Mc Namara MJ, Percy JP, Fielding IR. A manometric study of anal fissure treated by subcutaneous lateral internal sphincterotomy. *Ann Surg* 1990;211:235–8.
- [4] Xynos E, Tzortzinis A, Chryso E et al. Anal manometry in patients with fissure-in-ano before and after internal sphincterotomy. *Int J Colorectal Dis* 1993;8:125–8.
- [5] Nelson RL. Meta-analysis of operative techniques for fissure-in-ano. *Dis Colon Rectum* 1999;42:1424–8.
- [6] Weaver RM, Ambrose NS, Alexander-Williams J, et al. Manual dilatation of the anus vs. lateral subcutaneous sphincterotomy in the treatment of chronic fissure-in-ano. Results of a prospective, randomized, clinical trial. *Dis Colon Rectum* 1987;30:420–3.
- [7] Abcarian H. Surgical correction of chronic anal fissure: results of lateral internal sphincterotomy vs. fissurectomy-midline sphincterotomy. *Dis Colon Rectum* 1980;23:31–6.
- [8] Leong AF, Seow-Choen F. Lateral sphincterotomy compared with anal advancement flap for chronic anal fissure. *Dis Colon Rectum* 1995;38:69–71.
- [9] Nyam DC, Pemberton JH. Long-term results of lateral internal sphincterotomy for chronic anal fissure with particular reference to incidence of fecal incontinence. *Dis Colon Rectum* 1999;42:1306–10.
- [10] Mínguez M, Melo F, Espí A, et al. Therapeutic effects of different doses of botulinum toxin in chronic anal fissure. *Dis Colon Rectum* 1999;42:1016–21.
- [11] Jost W. Ten years' experience with botulin toxin in anal fissure. *Int J Colorectal Dis* 2002;17:287–97.

- [12] Brisinda G, Maria G, Bentivoglio AR, et al. A comparison of injections of botulinum toxin and topical nitroglycerin ointment for the treatment of chronic anal fissure. *N Engl J Med* 1999;341:65–9.
- [13] Maria G, Brisinda G, Bentivoglio AR, et al. Influence of botulinum toxin site of injections on healing rate in patients with chronic anal fissure. *Am J Surg* 2000;179:46–50.
- [14] Brisinda G, Maria G, Sganga G, et al. Effectiveness of higher doses of botulinum toxin to induce healing in patients with chronic anal fissures. *Surgery* 2002;131:179–84.
- [15] Richard CS, Gregoire R, Plewes EA, et al. Internal sphincterotomy is superior to topical nitroglycerin in the treatment of chronic anal fissure: results of a randomized, controlled trial by the Canadian Colorectal Surgical Trials Group. *Dis Colon Rectum* 2000;43:1048–57.
- [16] Evans JE, Luck A, Hewett P. Glyceryl trinitrate vs lateral sphincterotomy for chronic anal fissure. Prospective, randomized trial. *Dis Colon Rectum* 2001;44:93–7.
- [17] Maria G, Sganga G, Civello IM, et al. Botulinum neurotoxin and other treatments for fissure-in-ano and pelvic floor disorders. *Br J Surg* 2002;89:950–61.
- [18] Klein AW. Complications and adverse reactions with the use of botulinum toxin. *Semin Cutan Med Surg* 2001;20:109–20.
- [19] Jorge JMN, Wexner SD. Etiology and management of fecal incontinence. *Dis Colon Rectum* 1993;36:77–97.
- [20] Mentis BB, Irkorucu O, Akin M, et al. Comparison of botulinum toxin injection and lateral internal sphincterotomy for the treatment of chronic anal fissure. *Dis Colon Rectum* 2003;46:232–7.
- [21] Maria G, Brisinda G, Bentivoglio AR, et al. Botulinum toxin injections in the internal anal sphincter for the treatment of chronic anal fissure. Long-term results after two different dosage regimens. *Ann Surg* 1998;228:664–9.
- [22] Minguez M, Herreros B, Espi A, et al. Long-term follow-up (42 months) of chronic anal fissure after healing with botulinum toxin. *Gastroenterology* 2002;123:112–7.
- [23] Pitt J, Willilams S, Dawson PM. Reason for failure of glyceryl trinitrate treatment of chronic fissure-in-ano. A multivariate analysis. *Dis Colon Rectum* 2001;44:864–7.
- [24] Eckardt VF, Schnitt T, Bernhard G. Anal ultra slow waves. A smooth muscle phenomenon associated with dyschezia. *Dig Dis Sci* 1997;42:2439–45.
- [25] Schouten WR, Blankensteijn JD. Ultra slow wave pressure variations in the anal canal before and after lateral internal sphincterotomy. *Int J Colorectal Dis* 1992;7:115–8.