

Randomized, Prospective Trial Comparing 0.25 Percent Glycerin Trinitrate Ointment and Anal Cryothermal Dilators Only with 0.25 Percent Glycerin Trinitrate Ointment and Only with Anal Cryothermal Dilators in the Treatment of Chronic Anal Fissure: A Two-Year Follow-Up

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PURPOSE: The objective of this study was to compare the efficacy of 0.25 percent glycerin trinitrate ointment in association with cryothermal anal dilators with 0.25 percent glycerin trinitrate ointment only and cryothermal anal dilators only. **METHODS:** A total of 48 patients suffering from chronic anal fissure were enrolled in this prospective, randomized study between January 2002 and December 2003: Group A, 16 patients were treated with 0.25 percent glycerin trinitrate ointment and also used cryothermal anal dilators; Group B, 16 patients were treated with 0.25 percent glycerin trinitrate ointment only; Group C, 16 patients were treated with cryothermal anal dilator use only.

All patients in each group followed the specified treatment protocol for six weeks. **RESULTS:** After seven weeks of treatment, the symptoms complained of were resolved in 15 patients (93.7 percent) in Group A, 12 patients (75 percent) in Group B, and 12 patients (78 percent) in Group C. After two years of follow-up, 14 patients (87.5 percent) in Group A, 9 patients (56.2 percent) in Group B, and 10 patients (62.5 percent) in Group C presented no recurrence of symptoms. No patient in any group reported serious side effects of the treatment proposed, and treatment did not have to be withdrawn in any of the randomized patients. No episodes of anal incontinence of gas or feces were recorded in the patients who had used the anal dilators. **CONCLUSIONS:** The combined treatment for chronic anal fissure proved to be efficacious, safe, and with statistically significant better results than the other treatments analyzed. [Key words: Chronic anal fissure; 0.25 percent glycerin trinitrate ointment; Cryothermal anal dilators; Anorectal pressure gauge]

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Fissure in its chronic form may be defined as an ulceration of the skin covering the distal tract of the anal passage, which usually extends from the

anal verge to near the dentate line. Although frequently reported in young people, its actual incidence cannot be easily defined.¹ In most cases it is located near the posterior midline, occurring anteriorly in only 10 to 15 percent of cases¹; their occurrence in other locations should raise the suspicion that they are a clinical sign of a systemic disease (anal cancer, chronic intestinal inflammatory disease, tuberculosis, Crohn's disease, syphilis, acquired immunodeficiency syndrome).

The physiopathology of chronic anal fissure has not been definitively classified. Most patients present high pressure values in the anal canal,²⁻⁵ probably secondary to anomalous activity of the internal sphincter.⁶

It is believed that elevated sphincter pressures might cause a decrease in the perfusion pressure to anoderm with consequent ischemic area at the posterior commissure,⁷ which would favor the development of chronic fissure. Other authors, however, formulated the hypothesis that the fissure becomes chronic secondary to an alteration in the vascularization of the posterior region of the anal canal⁸ and that the reduced blood flow causes abnormal pressure values inside the anal canal.⁹

The hypothesis that the presence of antiendothelial cell antibodies in the serum of patients with chronic anal fissure causes an ischemic area in the posterior commissure and hypertension in the anal canal¹⁰ is interesting, but not all patients with chronic anal fissure present anomalous anal canal pressure values.¹¹⁻¹³

Many treatment protocols have been proposed for the conservative treatment of chronic anal fissure, but all are characterized by a high rate of recurrence¹⁴ with an efficacy that is only slightly greater than a treatment with a placebo.¹⁵ The treatment of choice¹⁶ for the surgical management of refractory anal fissures is the internal lateral sphincterectomy, or, as it was recently proposed, the controlled lateral sphincterectomy, which seems capable of reducing the risk of incontinence.¹⁷ The procedure reduces the pathologically raised pressure profile within the anal canal.

As for the use of anal dilators on their own to conservatively treat chronic anal fissure, for which satisfactory results were reported in one published study,¹⁸ two randomized trials^{19,20} have shown that they do not seem to decrease the number of patients undergoing internal anal sphincterectomy.¹⁴ Because manual anal dilation can damage the sphincter apparatus in a high percentage of patients,^{21,22} this method has been abandoned to all intents and purposes.

The objective of this study was to compare the efficacy of 0.25 percent glycerin trinitrate ointment in association with cryothermal anal dilators by only applying 0.25 percent glycerin trinitrate ointment and only using cryothermal anal dilators during two years of follow-up.

PATIENTS AND METHODS

Between January 1, 2002 and December 31, 2003, 48 consecutive patients with chronic anal fissure were enrolled in this randomized, prospective trial. All enrolled patients were previously informed about the different treatments of the chronic anal fissure and the goals of the trial in which they were asked to participate. The participants also committed themselves to comply with the therapeutic protocol. The patients were randomly allocated into three groups by using GraphPad Software, Inc.[®], statistical software (San Diego, CA).

In Group A, 16 patients were treated with a 0.25 percent glycerin trinitrate ointment (Crema di Trinitrato di Glicerina 0.25 percent[®], Sofar, Milan, Italy) and with cryothermal anal dilators (Dilatan[®], Sapi Med, Alessandria, Italy). The anal dilator, Dilatan[®],

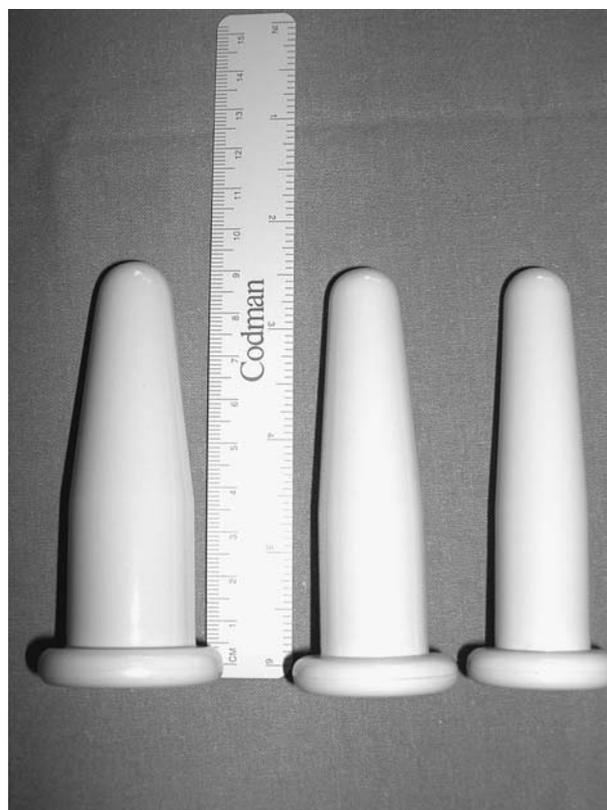


Figure 1. Anal cryothermal dilators

externally has a cylindrical shape, which becomes conical toward one end. The surface of the dilator is perfectly smooth. The internal compartment is hermetically sealed and contains a jelly capable of keeping heat (Fig. 1).

The 16 patients enrolled in Group B were treated only with 0.25 percent glycerin trinitrate ointment, whereas the 16 patients enrolled in Group C were treated only with the cryothermal anal dilators. The diagnosis of chronic anal fissure was based on the duration of symptoms for at least eight weeks: the presence of a fissure with hard edges and exposed fibers in the internal sphincter at the clinical examination, irrespective of the presence or absence of hypertrophic anal papilla and sentinel tag. Patients with systemic disease of which the anal fissure was a clinical manifestation and patients who had previously undergone surgery in the anorectal area or radiotherapy in the pelvic or perineal area were excluded. The enrolled patients underwent clinical assessment and anorectal manometry before starting the treatment.

The clinical assessment allowed the investigators to define the symptoms, duration, location, and classification of the fissure according to the extent that the internal sphincter fibers were exposed, according to the classification proposed by Kennedy *et al.*,²³ on a scale of zero to four: Grade 0 = healed; Grade 1 = fissure with exposed internal anal sphincter (IAS); Grade 2 = deeper fissure with widely exposed IAS; Grade 3 = deep undermined fissure; Grade 4 = deep undermined fissure associated perianal fistula.

The anorectal manometry was performed using a computerized system with 4.5-mm diameter water-perfused flexible probes with eight channels, arranged on the circumference, and a continuous and stationary pull-through procedure (The Polygraf™ ID multiparametric recorder with POLYGRAM NET® analysis software, Medtronic, Minneapolis, MN). The following parameters were considered: length of the sphincter area in millimeters, maximum resting pressure (MRAP) and maximum squeeze pressure (MSAP) in mmHg, presence of the rectoanal inhibitor reflex, and ultraslow wave activity.

Group A patients used the small anal dilator (20 mm) for the first week: the dilator was previously heated for 15 minutes by soaking in warm water at 40°C and using a standard mercury thermometer to check its temperature. To ease its introduction, patients lubricated the dilator with a gel with the active principles calendula, klamath weed, horse chestnut, wild chamomile, allantoin, and propolis (Dilatan crema®, Sapi

Med, Alessandria, Italy) and introduced it fully into the anal canal while the patient was lying on his or her side, and maintained in position for ten minutes. Shortly after extracting the dilator and a careful local cleansing, patients were instructed to apply a 0.5-g to 1-g dose of 0.25 percent glycerin trinitrate ointment to the edge and just inside the anus. This procedure was repeated twice per day: morning and evening. The protocol specified that the medium-sized dilator (23 mm) should be used in the second week, using the same procedure of the first week. Shortly after the extraction of the dilator and a careful local cleansing, patients were instructed to apply a 0.5-g to 1-g dose of 0.25 percent glycerin trinitrate ointment to the edge and just inside the anus. Starting from the third week and for a total of four weeks, the large dilator (27 mm) should be used, exactly as it has been provided for during the first two weeks, for a six-week treatment.

Group B patients were invited to apply a 0.5-g to 1-g dose of 0.25 percent glycerin trinitrate ointment to the edge and just inside the anus three times per day for six weeks. Group C patients were treated with anal dilator use only; the patients used the small anal dilator (20 mm) for the first week: the dilator was previously heated for 15 minutes according to the same operational procedure followed by patients in Group A. Later, to ease the introduction, they lubricated the dilator with gel (Dilatan crema®, Sapi Med, Alessandria, Italy) and introduced it fully into the anal canal while the patient was lying on his or her side and maintained in position for ten minutes. This procedure was repeated twice per day: morning and evening. The protocol specified that the medium-sized dilator (23 mm) should be used in the second week, and from the third week and for a total of four weeks, the large dilator (27 mm) should be used, as described above, for a total duration of treatment of six weeks.

The patients of each group were prescribed a fiber-rich diet with a bulking agent supplement (Psyllium plantago). At home, patients were instructed to record the evolution of symptomatology—the onset of side effects caused by glycerin trinitrate. Patients had to report a possible onset of migraine and its intensity, which was evaluated by use of a visual analog scale score for pain (0 = no pain to 10 = maximum pain). They also were asked to report onset and duration of tachycardia attacks as well as the compliance with the therapeutic protocol on an appropriate diary and to fill in a Wexner incontinence

score questionnaire²⁴; the diary had to be written daily for the whole duration of treatment and then on a weekly basis. During the two-year follow-up, patients were instructed to report the possible onset of disorders at any time.

All the patients were reassessed clinically one week after the end of the treatment with a clinical examination and an anorectal manometry. The patients whose symptoms were resolved and anoderma reepithelized were considered cured. Follow-up consisted of a clinical check 12 and 24 months after the end of treatment. During each visit, the diary and the questionnaire filled in by the patient were checked, a clinical evaluation was performed, and the possible onset of side effects was reported; a further anorectal manometry was performed only on those patients for whom the symptoms had not been resolved and/or who had suffered a recurrence of the condition. All patients enrolled in each group have terminated the follow-up as prescribed.

STATISTICAL ANALYSIS

Data were analyzed by using GraphPad Software Inc.[®], statistical software. The results are expressed as means \pm standard deviations.

The paired sample *t*-test was performed to compare the variation in MRAP and MSAP in the three groups before and after the clinical treatment. The values were considered statistically significant for $P < 0.01$.

One-way ANOVA test with Bonferroni's multiple comparison was performed to evaluate the variation in MRAP and MSAP in the three groups, before and after the proposed treatment. The values were considered statistically significant if $P < 0.05$. The percentage variations were analyzed by using the Fisher's exact test.

RESULTS

A total of 26 males (54 percent) and 22 females were enrolled; in 42 patients (87.5 percent) the fissure was located at the posterior commissure, 21 (43 percent) complained of pain and bleeding during defecation, 19 (39.5 percent) reported severe pain during defecation, and 8 (16.6 percent) complained of hematochezia. The objective examination detected the presence of a sentinel tag in 23 patients (47.9 percent) and a hypertrophic anal papilla in 20 (41.6 percent). Forty-two patients (87.5 percent) complained of constipation (score >15), which met the

criteria of the Cleveland Clinic Florida constipation scoring system²⁵: mean=18.36 (range, 15–24). All patients presented the rectoanal inhibitory reflex. The average length of the anal canal was 4 (range, 2–4) cm, and 38 patients (79.1 percent) presented ultraslow waves. Before the treatment, there were no statistically significant differences in the three groups in terms of patient characteristics, duration of symptoms, and pressure values ($P > 0.05$; Table 1).

One week after the end of treatment, the patients were reassessed and underwent a manometry test. In Group A, just 1 patient (6.2 percent) still experienced symptoms, and in the 15 cured patients there was a considerable reduction in the manometric pressure values (maximum resting pressure: from 123.8 ± 20.38 mmHg to 76.9 ± 10.36 mmHg, $P < 0.01$, *t*-test; maximum squeeze pressure: from 214.9 ± 40.5 mmHg to 152.2 ± 25.63 mmHg, $P < 0.01$, *t*-test).

In Group B, 3 patients (18.7 percent) still experienced symptoms, and in the 12 cured patients there was a considerable reduction in the manometric pressure values (maximum resting pressure: from 129.4 ± 18.74 mmHg to 96.69 ± 17.25 mmHg, $P < 0.01$, *t*-test; maximum squeeze pressure: from 218.4 ± 37.5 mmHg to 168.5 ± 26.41 mmHg, $P < 0.01$, *t*-test). In addition, one patient (6.2 percent) presented partial reepithelization of the fissure but reported no symptoms.

Finally, in Group C, 3 patients (18.7 percent) complained that the symptoms persisted, and in the 12 cured patients there was a considerable reduction in the manometric pressure values (maximum resting pressure: from 125.9 ± 22.53 mmHg to 94.5 ± 18.74 mmHg, $P < 0.01$, *t*-test; maximum squeeze pressure: from 227.5 ± 41.34 mmHg to 172.4 ± 25.51 mmHg, $P < 0.01$, *t*-test; Table 2). One patient in Group C (6.2 percent) showed a persistent fissure but no symptoms.

Of the nonresponders, one patient (6.2 percent) in Group A, three patients (18.7 percent) in Group B, and three patients (18.7 percent) in Group C, presented persistently high manometric pressure values at the end of treatment, and no significant variation in pressure values before and after treatment occurred in any of these patients ($P > 0.01$, *t*-test; Table 3).

At the clinical follow-up one year after the end of treatment, 15 patients (93.7 percent) in Group A, 11 patients (68.7 percent) in Group B, and 12 patients (75 percent) in Group C were clinically cured and reported no symptoms. At the two-year, follow-up visit, 14 patients (87.5 percent) in Group A, 9 patients (56.2 percent) in Group B, and 10 patients (62.5

Table 1.
Characteristics of Patients Before Treatment

Characteristics	Group A (n = 16)	Group B (n = 16)	Group C (n = 16)	P Value
Male/female ratio	7/9	10/6	9/7	
Mean age (yr)	28.94 (14–42)	26.19 (14–44)	23.13 (13–41)	NS ^a
Mean symptoms duration (mo)	17.5 (6–31)	16.88 (8–34)	15.19 (7–31)	NS ^a
Fissure position				
Posterior midline	14 (87.5)	15 (93.7)	13 (81.2)	
Anterior midline	2 (12.5)	1 (6.25)	3 (18.7)	
Pain	6 (37.5)	5 (31.2)	8 (50)	NS ^a
Bleeding	4 (25)	3 (18.7)	1 (6.2)	NS ^a
Pain and bleeding	6 (37.5)	8 (50)	7 (43.7)	NS ^a
Sentinel pile	7 (43.7)	9 (56.2)	7 (43.7)	NS ^a
Anal papilla	5 (31.2)	7 (43.7)	8 (50)	NS ^a
Sentinel pile and anal papilla	4 (25)	0	1 (6.2)	NS ^a
Constipation	14 (87.5)	15 (93.7)	13 (81.25)	NS ^a
Fissure score ^b				
Grade 1	4 (25)	7 (43.7)	6 (37.5)	NS ^a
Grade 2	9 (56.2)	8 (50)	6 (37.5)	NS ^a
Grade 3	3 (18.7)	1 (6.2)	4 (25)	NS ^a

Data are numbers with percentages or ranges in parentheses.

Group A: 0.25 percent glycerin trinitrate ointment and anal dilators; Group B: 0.25 percent glycerin trinitrate ointment; Group C: anal dilators.

^aOneway ANOVA with Bonferroni's multiple comparison test between the three groups, before treatment (NS = $P > 0.05$).

^bFissure grade: Grade 1: fissure with exposed internal anal sphincter; Grade 2: deeper fissure with widely exposed internal anal sphincter; Grade 3: deep undermined fissure.

percent) in Group C reported no recurrence of symptoms (Table 4). No patient reported continence disorders: mean 0.54 (range, 0–2), evaluated according the Cleveland Clinic Florida Fecal Incontinence (CCF-FI) scoring system.²⁴

In the Group A patient in whom there was a recurrence at the two-year, follow-up assessment, the manometric test showed that the pressure values

were greater (MRAP=118 mmHg and MSAP=182 mmHg) than the values recorded after the treatment (MRAP=81 mmHg and MSAP=151 mmHg) but still lower than those recorded at the baseline (MRAP=148 mmHg, MSAP=257 mmHg).

For the Group B patient who reported a recurrence at the one-year, follow-up assessment, the manometric test showed that the pressure values were higher

Table 2.
Anorectal Physiology Result Before and After Treatment

Anorectal Physiology Results	Group A (n = 16)	Group B (n = 16)	Group C (n = 16)	P Value
Before treatment				
Maximum resting pressure (mmHg)	123.8 ± 20.38	129.4 ± 18.74	125.9 ± 22.53	> 0.05 ^a
Maximum squeeze pressure (mmHg)	214.9 ± 40.5	218.4 ± 37.5	227.5 ± 41.34	> 0.05 ^a
Sphincter length (cm)	4 (2–4)	4 (2–4)	4 (2–4)	
Inhibitory rectoanal reflex	present	present	present	
After treatment				
Maximum resting pressure (mmHg)	76.9 ± 10.36	96.69 ± 17.25	94.5 ± 18.74	< 0.05 ^b
Maximum squeeze pressure (mmHg)	152.2 ± 25.63	168.5 ± 26.41	172.4 ± 25.51	> 0.05 ^a
Sphincter length (cm)	4 (2–4)	4 (2–4)	4 (2–4)	
Inhibitory rectoanal reflex	present	present	present	

Data are presented in mmHg and values are means ± standard deviations or numbers with ranges in parentheses.

Group A: 0.25 percent glycerin trinitrate ointment and anal dilators; Group B: 0.25 percent glycerin trinitrate ointment; Group C: anal dilators.

^aOneway ANOVA with Bonferroni's multiple comparison test between the three groups, before and after treatment (NS = $P > 0.05$).

^bOneway ANOVA test between the three groups after treatment (NS = $P > 0.05$).

Table 3.
Anorectal Physiology Result Before and After Treatment in Patient Nonresponders

Group	Patient	Gender	Age (yr)	Before		After	
				MRAP (mmHg)	MSAP (mmHg)	MRAP (mmHg)	MSAP (mmHg)
A	P.S.	F	32	156	259	100	210
B	Z.M.	F	31	111	205	90	149
	T.A.	F	24	148	225	97	146
C	S.S.	M	31	159	234	135	145
	C.E.	M	23	163	198	111	104
	D.C.M.	F	19	147	246	91	179
		M	15	161	221	123	146

MRAP=maximum resting anal pressure; MSAP=maximum squeeze anal pressure; M=male; F=female.

(MRAP=123 mmHg and MSAP=175 mmHg) than the values recorded after the treatment (MRAP=97 mmHg and MSAP=168 mmHg) but still lower than those recorded at the start (MRAP=149 mmHg, MSAP=189 mmHg). A similar trend in pressure values was observed in the other three patients (18.7 percent) who suffered recurrences of the symptoms at the two-year follow-up; the values were always lower than those recorded before treatment.

No Group C patient reported any recurrence after one year, whereas two patients (12.5 percent) reported recurrence of the symptoms at the follow-up two years after the end of treatment, with a similar trend in the pressure values.

The patients of each group developing a recurrence of symptomatology received 20 units of botulinum toxin A diluted in saline to a concentration of 50 units/ml. A total of 0.4 ml of solution was injected with a 22-gauge needle into the intersphincteric groove in the direction of the internal anal

sphincter. No patients showed episodes of incontinence (score = 0), according to the Cleveland Clinic Florida Fecal Incontinence (CCF-FI) scoring system.²⁴

The second recurrence of symptomatology in a patient enrolled in Group B and in a patient enrolled in Group C prompted us to perform a surgical lateral internal sphincterotomy. All patients have terminated the expected therapeutic treatment; they have been informed by phone about follow-up visits to take place after one month to agree on a suitable time. By use of this procedure, no patient missed the follow-up.

DISCUSSION

The treatment of chronic anal fissure is still open to debate. Surgery is the most widely used approach to resolve the spasm of the internal sphincter, and during the years, many techniques have been proposed.²⁶ Anal sphincterectomy can expose the patient to the risk of anal incontinence²⁷⁻²⁹ and still

Table 4.
Clinical Results of Treatment in the Three Groups

Symptoms	Group A (n = 16)	Group B (n = 16)	Group C (n = 16)
Pain	0	1 (6.2)	0
Bleeding	0	0	0
Pain and bleeding	1 (6.2)	2 (12)	3 (18.7)
Gas incontinence	0	0	0
Fecal soiling	0	0	0
Fecal incontinence	0	0	0
Asymptomatic persistence	0	1 (6.2)	1 (6.2)
Symptomatic persistence	1 (6.2)	3 (18.7)	3 (18.7)
Healing of fissure at seven weeks	15 (93.7)	12 (75)	12 (75)
Healing at one-year follow-up	15 (93.7)	11 (68.7)	12 (75)
Healing at two-year follow-up	14 (87.5)	9 (56.2)	10 (62.5)
Recurrence at one-year follow-up	0	1 (6.25)	0
Recurrence at two-year follow-up	1 (6.2)	3 (18.7)	2 (12.5)

Data are numbers with percentages in parentheses.

Group A: 0.25 percent glycerin trinitrate ointment and anal dilators; Group B: 0.25 percent glycerin trinitrate ointment; Group C: anal dilators.

has a risk of recurrence, mainly caused by inadequate sectioning of the internal sphincter.³⁰ Manual anal dilation has been considered the primary treatment for chronic anal fissure for many years. However, many studies have queried its efficacy for the high rate of incontinence associated with it, caused by sphincter damage.^{1,21,22} An online search of the National Library of Medicine PubMed search engine (www.nlm.nih.gov) using the research key, "anal dilators in treatment of anal fissure," produced little evidence of the efficacy of anal dilators, which do not seem to influence the total number of patients undergoing surgical procedures.^{15,18,19,26}

Medical treatment of chronic anal fissure also results in lower recovery rates and a higher rate of recurrences than surgery.^{1,17} The use of glycerin trinitrate temporarily reduces the tone of the internal sphincter, and thus of the maximum resting pressure, with a recovery rate that is slightly higher than a placebo.^{15,31} The role of glycerin trinitrate remains uncertain: the persistence of symptoms for more than six months and the presence of a sentinel tag may be responsible for the failure of medical treatment with trinitrate.²² Finally, the fact that many patients report episodes of tachycardia³² and headaches of such intensity that they cause them to stop treatment earlier than planned should not be ignored.^{32,33} To reduce side effects, the dosage of glycerin trinitrate has been reduced to 0.25 percent, which seems to offer the same therapeutic effects as the 0.5 percent dosage of the drug with fewer side effects.^{32,34}

The rationale for the use of anal dilators is the finding that they induce muscle relaxation with a consequent reduction in sphincter hypertonia.¹⁸ The muscle relaxing effect is enhanced when the dilator is heated, resulting in a synergy that reduces muscle tone.

This study was designed to demonstrate the efficacy of the association of anal dilators and glycerin trinitrate in the treatment of chronic anal fissure and to assess whether the proposed association allows us to further reduce the glycerin trinitrate dose to minimize side effects and enhance patient compliance.

All the patients enrolled in this study presented high maximum resting pressure values. The evaluation of pressure values, at the end of treatment, allowed us to assess that in Group A, a remarkable reduction in pressure values had been recorded compared with those recorded before the treatment (mean MRAP = 76.9 ± 10.36). In Group B, the reduction in pressure values had been lower (mean MRAP = 96.69 ± 17.25) and a similar result has been

reported in patients of Group C (mean MRAP = 94.5 ± 18.74). Statistical comparison of the decrease in the mean maximum anal resting pressure values in the three groups after treatment showed that there were statistically significant differences between Group A and Group B, and between Group A and Group C ($P < 0.01$), whereas there was no significant difference between the mean falls in pressure values in Group B and Group C ($P > 0.01$).

The change in MSAP after treatment in each group was statistically significant, although the reduction in these pressure values was higher in the patients in Group A (mean MSAP = 152.2 ± 25.63) compared with the patients in Group B (mean MSAP = 168.5 ± 26.41) and Group C (mean MSAP = 172.4 ± 29.8). Statistical comparison of the decrease in the mean maximum squeeze pressure values in the three groups after treatment showed that there were no significant differences ($P > 0.01$).

The reduction in pressure values and the persistence of these values within the range of normality for patients in Group A is correlated with the synergic action of the glycerin trinitrate and the dilators, which are together able to induce a statistically significant reduction in pressure values compared with the patients in the other groups. It may be plausibly suggested that the subsequent application of ointment helps to maintain the resulting muscle relaxation by use of the anal dilator.

Slow waves, which represent the baseline electric activity of the internal anal sphincter, were encountered in the patients in all three groups, and their presence was more prolonged than in the control population. The most interesting aspect was the finding that the reduction in the time for which these waves persist was greater in Group A than in Group B or Group C. In fact, 6.2 percent of the patients in Group A and 18.7 percent of the patients in Group B and Group C presented no resolution of the symptom and maintained high sphincter hypertonia both at rest and when contracted.

These data would seem to confirm that sphincter hypertonia represents the principal element in the pathogenesis of chronic anal fissure, although we cannot clarify the etiopathogenetic mechanisms of chronic anal fissure, or, above all, whether as yet unknown etiologic elements also are involved.

The follow-up allowed us to establish that one year after treatment 93.7 percent of patients in Group A compared with 68.7 percent of patients in Group B and 75 percent of patients in Group C had developed

no symptoms of recurrence, and one year later we recorded decreases of 56.2 and 62.5 percent in the cured rate in Groups B and C respectively, whereas the number of cured patients in Group A remained the same. None of the patients treated reported fecal incontinence, which was the reason that we did not perform transanal ultrasound scanning with a rotating probe. Therefore, the use of anal dilators is not associated with any impact on anal continence. In this respect, to avert the risk of sphincter lesions and to facilitate introduction of the dilator, patients were always invited to start with the smallest diameter device and to warm it before use. No patient in Group A or Group C reported problems using the anal dilators. Headache secondary to the use of glycerin trinitrate was encountered in 18.7 percent of the patients treated with nitroglycerin alone, and no headaches occurred in the patients in Group A: this must be a consequence of the fact that the patients in Group A received a lower dosage of nitroglycerin than the patients in Group B. However, the headaches were not so severe as to cause suspension of the treatment. No cases of tachycardia requiring therapeutic measures and/or suspension of the treatment were recorded.

CONCLUSIONS

Treatment of chronic anal fissure using anal dilators and 0.25 percent glycerin trinitrate seems capable of inducing a long-lasting cure. The treatment protocol does not cause continence disorders and minimizes the risk of the headache, which is a side effect of nitrate use. The use of previously warmed anal dilators of increasing diameter does not seem to cause sphincter lesions, and this is related to the capacity of the muscle structures to adapt.

Patients with abnormal pressure values in the anal channel at rest and while squeezing might not obtain any benefit from the proposed protocol, because they do not obtain any benefit from the conservative treatments whose efficacy is now considered to be slightly better than that of a placebo.^{16,34,35} However, the data that emerged from this study need further evaluation and confirmation in the form of randomized trials involving greater numbers of patients. The analyzed treatment program could significantly decrease the number of patients undergoing anal sphincterectomy.

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