A Comparative Study between the Use of Topical Glyceryl Trinitrate Versus Surgical Internal Sphincterotomy for Treatment of Chronic Anal Fissure

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Abstract

Background: The anal fissure is one of the most frequent proctologic problems that affect many patients altering their social and work lives as well. Consequently, it is important to make a proper diagnosis and apply a rapid and effective treatment. It usually starts as a linear tear in the anal canal mucosa, and if healing fails, it evolves into a Chronic Anal Fissure (CAF).

Objective: To make a comparison between the use of topical glyceryl trinitrate and surgical internal sphincterotomy for treatment of CAF.

Patients and Methods: This prospective study included forty patients with CAF divided into two equal groups: The first group underwent surgical treatment in the form of Subcutaneous Lateral Internal Sphincterotomy (SLIS), and the second group used the topical treatment in the form of 0.2% glyceryl trinitrate applied twice daily for six weeks. All the patients came to general surgery outpatient clinics at the 6th of October Health Insurance Hospital at Cairo, in the period from May to December 2016. Follow-up was done at regular pre-specified intervals and two main outcomes were outlined: “Fissure healing” and “pain relief” to compare between both groups.

Results: In the first group with surgical treatment, fissure healing rates were as the following: (20%) by 4 weeks, (80%) by 6 weeks and (100%) by 8 weeks. Pain relief rates were (90%) by 2 weeks postoperatively and (100%) by the end of 4th week. With regard to post-operative complications, (65%) of cases had post-operative discharge, (35%) had incontinence to gases but not to stool (0%). And (20%) had pruritis during the first 2 weeks. For the second group subjected to topical treatment, fissure healing rates were (20%) by 4 weeks, (70%) by 6 weeks and (85%) by 8 weeks. Pain relief rates were (65%) by 2 weeks and (100%) by 4 weeks. Regarding treatment-related side effects, headache (45%) was the commonest problem, anal itching (35%), three patients (15%) failed to heal and two patients (10%) had recurrence within 6 months. This study has a non significant p-value for the outcome difference between both groups regarding fissure healing and pain relief.

Conclusion: Topical glyceryl trinitrate should still be considered as a first line treatment for CAF, it is safe and produces chemical sphincterotomy without the complications of surgery, plus it is specially useful for patients with recurrent CAF after previous surgical treatment and those unfit or unwilling to undergo surgery. Surgical SLIS should be spared for those who fail conservative topical treatment.


Introduction

ANAL fissure is a linear tear in the anal canal mucosa. If healing fails, it evolves into a Chronic Anal Fissure (CAF). This is one of the most frequent proctologic problems affecting younger patients mainly, affecting both their social and work lives. As it is a disabling disease, it is important to make a proper diagnosis and apply a rapid and efficient treatment. At present, there are different therapeutic choices, both medical and surgical, Among the first, there are several options that relax the Internal Anal Sphincter (IAS), one of them which is the most used is topical 0.2% glyceryl trinitrate ointment. There being some randomized controlled studies reporting 48% and 69% healing rates and other studies with comparable results against surgery [1].

It is proposed that elevated Internal Anal Sphincter (IAS) pressure may cause ischemia of the

Abbreviations:

CAF : Chronic Anal Fissure.
SLIS : Subcutaneous Lateral Internal Sphincterotomy.
NO : Nitric Oxide.
IAS : Internal Anal Sphincter.
anal lining and this may be responsible for the pain of anal fissures and their failure to heal. When conservative pharmacologic therapy fails or fissures recur frequently, surgical sphincterotomy is the surgical treatment of choice [2].

Lateral internal sphincterotomy results in complete healing of the fissure in 92-99% of patients. But impaired continence of flatus and liquid stool is sometimes reported, but this is nearly always temporary [3,4].

Topical treatment is effective in patients with CAF, at short-term and long-term periods. Because for many patients it is not a definitive therapy, it can be offered to those who are ready to receive repeated treatments. Longer intervals between symptoms appearance and treatment initiation negatively affects fissure healing and recurrence rate [5].

The goal of medical treatment for CAF is to achieve a temporary reduction of pressure in the anal canal, mainly the IAS, to facilitate the healing of the fissure (reversible sphincterotomy) thereby reducing muscle tone. Various mechanisms can be used; increasing Nitric Oxide (NO), direct depletion of intracellular calcium, stimulation of muscarinic receptors, inhibition of alpha-adrenergic receptors, or stimulation of beta-adrenergic receptors [6]. Recognition of NO as a non-adrenergic, non-cholinergic neurotransmitter mediating IAS relaxation has initiated a wide use of nitrates in treatment of CAF [7].

Many anal fissures heal with topical treatment with glyceryl trinitrate. LIS remains effective but should be preserved for patients who fail to respond to initial chemical sphincterotomy [8].

It is the aim of this work to present a comparison between the use of surgical treatment in the form of SLIS (Group A), and the use of chemical sphincterotomy via topical 0.2% glyceryl trinitrate (Group B).

Patients and Methods

This prospective study included forty patients in General Surgery Outpatient Clinics of “the 6th of October Health Insurance Hospital” diagnosed to have a chronic anal fissure (persistent complaint for more than two months).

Patients with chronic anal fissure were randomly selected regardless the age or sex, as shown in (Table 1) about age distribution. The study included three stages; early assessment stage, treatment stage and post-treatment follow-up stage in a period of six months from June to December, 2016.

Inclusion criteria:
- Patients with chronic anal fissure (persisting for at least two months duration).
- Patients with age ranging from 16-70 years.
- Both males and females.
- Patients with failed medical treatment (for applying surgical approach).
- Patients with failed surgical treatment (for applying medical approach).

Exclusion criteria:
- Patients with acute anal fissure (duration less than two months).
- Age less than 15 years or more than 70 years.
- Pregnant females.
- Patients diagnosed with inflammatory bowel disease.
- Patients under treatment with nitrates for ischemic heart diseases.

Patients were divided into two equal Groups A & B as follows:

Group A: Twenty patients treated by surgical treatment in the form of Subcutaneous Lateral Internal Sphincterotomy (SLIS). All patients had undergone necessary pre-operative assessment including full history taking, routine pre-operative laboratory investigations and written consent. In operative theaters, all patients received spinal anesthesia via heavy marcaine though some cases needed propofol-based sedation to overcome apprehension. The lithotomy position was used for all patients. Prepping with betadine antiseptic and draping were done.

Technique: After testing for sensation loss by spinal anaesthesia, a lateral one-two centimeters long circumferential anal incision was made in the cutaneous margin of anal canal over lower edge of the internal sphincter. Then the skin was dissected from the internal sphincter by a curved forceps and minimal dissection of intersphincteric plane was done. Thus the internal sphincter was isolated and clearly seen. The lower two centimeters of internal sphincter were divided, so the technique used was “incomplete sphincterotomy”. Careful hemostasis was made via monopolar diathermy. No stitches taken and an anal pack was inserted for at least six hours postoperatively. Proper analgesics were used. All patients were discharged on
follow-up criteria:

Patients were followed-up in the General Surgery Outpatient Clinic at two weeks interval for the following:
- Pain relief.
- Fissure healing.
- Post-operative complications.
- Recurrence within six months.

Group B: Another twenty patients were subjected to topical application of 0.2% GTN for six weeks. A regimen of about 500mg, equivalent to 0.5cc, applied twice daily all around the anal verge. Patients were allowed to withdraw from the trial at any time.

Follow-up criteria:

Patients were followed-up in General Surgery Outpatient Clinic after exclusion of complications, with clear advice about home treatment in the form of antibiotics (gram negative and anerobes specific), analgesics and dietary recommendation consisting of soft diet during the first week together with plenty of vegetables and bulking agents such as bran containing diet. Clinical assessment in the outpatient clinic was repeated at regular predetermined intervals to compare the pre-operative condition.

Statistical analysis:

Data was analyzed using SPSS (Statistical Package for Social Sciences) Version 16. Qualitative data were presented as number and percent. Comparison between groups was done by Chi-square test. p-values less than 0.05 were considered to be statistically significant. In this study, the p-value was considered non significant for both fissure healing and pain relief while comparing both groups.

Results

In Group A, the surgical treatment showed fissure healing rates of (20%) by 4 weeks post-operatively, (80%) by 6 weeks and (100%) by the end of 8 weeks after surgery. Pain relief was achieved by (90%) within 2 weeks. Two patients only showed prolonged pain that ended within next two weeks without complications.

With regard to post-operative complications, discharge was reported in (65%) of patients, which stopped one week after the surgery. Incontinence to flatus occurred in (35%) of patients but not to stool (0%). This problem was reported during the first 3 weeks post-operatively before continence restored by the fourth week. Pruritis during the
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The first ten days was also reported in (20%) of patients. No recurrence occurred during the whole period of six months on follow-up.

For the group treated by topical glyceryl trinitrate, Group B, this study showed fissure healing rates of (20%) within 4 weeks, (70%) by 6 weeks and (85%) at the end of 8th week of treatment. Pain relief had a rate of (65%) within 2 weeks and (100%) at the end of 4th week.

A single case recorded severe anal irritation on first-time application that hardly improved with topical anaesthetic ointment and oral non-steroidal anti-inflammatory medication. This patient refused further treatment and was therefore excluded from the study. With regard to treatment-related side effects, the main problem was headache (45%) that was temporary within the first week of application and ranged from mild to severe. But interestingly this did not affect the compliance to treatment and the patient resumed application of topical glyceryl trinitrate in the specified course of six weeks. Anal itching (35%) was the second problem but it was also transient and did not affect the compliance. Two cases (10%) had recurrence of anal fissure within six months and three patient (15%) failed to heal with topical treatment.

Table (2): Table showing incidence of post-operative complications in Group A.

<table>
<thead>
<tr>
<th>Complications</th>
<th>Number of patients (n=20)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bleeding</td>
<td>0</td>
</tr>
<tr>
<td>Discharge</td>
<td>13</td>
</tr>
<tr>
<td>Pruritis</td>
<td>4</td>
</tr>
<tr>
<td>Incontinence to gases only</td>
<td>7</td>
</tr>
<tr>
<td>Incontinence to stool</td>
<td>0</td>
</tr>
<tr>
<td>Symptoms persistent</td>
<td>0</td>
</tr>
<tr>
<td>Recurrence within 6 months</td>
<td>0</td>
</tr>
</tbody>
</table>

For the group treated by surgical sphincterotomy, Group A, this study showed fissure healing rates of (20%) within 4 weeks, (60%) by 6 weeks and (84%) at the end of 8th week of treatment. Pain relief had a rate of (65%) within 2 weeks and (100%) at the end of 4th week.

A single case recorded severe anal irritation on first-time application that hardly improved with topical anaesthetic ointment and oral non-steroidal anti-inflammatory medication. This patient refused further treatment and was therefore ruled out of the study. With regard to treatment-related side effects, the main problem was headache (45%) that was temporary within the first week of application and ranged from mild to severe. But interestingly this did not affect the compliance to treatment and the patient resumed application of topical glyceryl trinitrate in the specified course of six weeks. Anal itching (35%) was the second problem but it was also transient and did not affect the compliance. Two cases (10%) had recurrence of anal fissure within six months and three patient (15%) failed to heal with topical treatment.

Table (3): Table comparing fissure healing in both groups with non significant \( p \)-value.

<table>
<thead>
<tr>
<th>Fissure healing</th>
<th>4 weeks</th>
<th>6 weeks</th>
<th>8 weeks</th>
<th>No healing</th>
<th>( \chi^2 )</th>
<th>( p )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>4</td>
<td>12</td>
<td>4</td>
<td>0</td>
<td>3.325</td>
<td>0.068</td>
</tr>
<tr>
<td>Group B</td>
<td>4</td>
<td>10</td>
<td>3</td>
<td>3</td>
<td>0.344</td>
<td>0.568</td>
</tr>
</tbody>
</table>

Fig. (5): A comparison of time of fissure healing in both groups.

Table (4): Table comparing pain relief in both groups with non significant \( p \)-value.

<table>
<thead>
<tr>
<th>Pain relief</th>
<th>2 weeks</th>
<th>4 weeks</th>
<th>( \chi^2 )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td>18</td>
<td>2</td>
<td>3.584</td>
</tr>
<tr>
<td>Group B</td>
<td>13</td>
<td>7</td>
<td>0.0583</td>
</tr>
</tbody>
</table>

Fig. (6): A comparison of time of pain relief in both groups.
Discussion

In this prospective study, randomly selected forty patients with chronic anal fissure who came to General Surgery Outpatient Clinics at “the 6th of October Health Insurance Hospital” in the period from May to December 2016. They were divided into two equal groups, Group A was assigned for surgical treatment in the form of Subcutaneous Lateral Internal Sphincterotomy (SLIS).

The second group, Group B, were subjected to medical treatment in the form of topical 0.2% glyceryl trinitrate, applied on a regimen of 0.5cc (equivalent to about 500mg) twice daily all around the anal verge. All patients were allowed to withdraw from the trial at any time.

Aslam et al., [9] in a similar study published, showed that surgical LIS had a fissure healing rate of (93%) within 6 weeks. Only one patient (3.3%) reported persistent pain post-operatively for about 6 weeks. Two patients (6.6%) reported persistent bleeding per rectum, which is the same number of cases reported incontinence, but the study did not demonstrate whether to flatus or to stool. On the other hand, topical treatment showed fissure healing by only (50%) in 6 weeks with (56%) pain relief. Headache as a side effect had a rate of (66%).

El-Labban et al., [10], demonstrated that surgical LIS in twenty patients with CAF had healing rate of (50%) within 2 weeks, (90%) after 4 weeks and (95%) after 6 weeks with reduction in pain score from 100 to 40 at 4 weeks, to 20 at 6 weeks and finally to 0 after 8 weeks. Headache rate was reported in (7.5%) of cases within 2 weeks standing incontinence for three months after the procedure. Topical glyceryl trinitrate had reported fissure healing rates of (15%) at 2 weeks, (25%) at 4 weeks, (40%) at 6 weeks and (70%) at 8 weeks. Pain score reduction from 100 to 10 by 2 weeks, to 40 at 4 weeks, to 20 at 6 weeks and finally to 0 at 8 weeks. Headache reported by (65%) of cases. Only one case had recurrence of anal fissure after three months follow-up.

Jan et al., [11] another study, including seventy cases, showed fissure healing rates with surgical LIS of (74%) within 4 weeks and (85%) at the end of 6th week. With pain relief by (68%) within 2 weeks and (85%) after 6 weeks. Bleeding per rectum was the most apparent complication (20%). Incontinence to flatus was reported in five patients (14%) that subsided at the end of 8th week. Wound infection (8%) was also reported. The group treated by topical glyceryl trinitrate demonstrated fissure healing rates of (0%) by 2 weeks, (25%) by 4 weeks, (62%) by 6 weeks and (74%) by the end of 8th week. Pain relief rates were (40%) by 2 weeks, (60%) by 4 weeks, (80%) by 6 weeks and same at 8 weeks. Headache rate was (11%).

Conclusion:

It should be established that, topical glyceryl trinitrate is basically safe and can still be used as first line treatment for chronic anal fissure. It produces chemical sphincterotomy without the complications related to surgery and it is specifically useful for patients with recurrent fissure after previous surgical sphincterotomy and also for those unfit or unwilling to undergo surgical treatment. Surgical SLIS should be spared for those who fail conservative topical treatment.

References

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