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## Research Article

# Comparative Study of Glyceryl Trinitrate Ointment versus Lateral Internal Sphincterotomy in Management of Chronic Anal Fissure

### Abstract

**Aims and Objectives:** To prospectively evaluate and compare effectiveness of topical 0.2% glyceryl trinitrate ointment vs lateral internal sphincterotomy in treatment of patients with chronic anal fissure.

**Material and Methods:** The study included a total of 50 patients presented with chronic anal fissure, divided into two groups by computer generated randomization. Group A included 25 patients with chronic anal fissure treated with local glyceryl trinitrate ointment 0.2% whereas Group B included 25 patients managed by lateral internal sphincterotomy.

**Results:** The mean age of patients in group A was 34.6±12.8 years and in Group B was 32.12±11.57 years ( $p > .05$ ). In group A, out of 25 patients, 19 were male and 6 females, whereas in group B, there were 20 males and 5 females. The mean pain score of patients before treatment in group A was 8.64±0.95 where as in group B was 8.44±1.19. At the end of six weeks of treatment the mean pain score was 1.64±2.43 in group A and 0.24±1.20 in group B respectively. Complete healing was observed in 18 out of 25 (72%) patients in group A whereas all 25 (100%) patients in group B had completely healed fissures at the end of six weeks. Except headache which was reported in 9 out of 25 (36%) patients in group A no other side effect was seen in this group. Whereas only 1 out of 25(4%) patients in group B developed haematoma in the perianal area, which was relieved conservatively within 1 week.

**Conclusion:** Glyceryl trinitrate ointment is a good alternative mode of therapy, hence lateral internal sphincterotomy may be reserved for patients who fail to respond to initial glyceryl trinitrate therapy..

## Introduction

Anal fissure is a painful linear mucosal tear situated in distal anal canal extending from just below dentate line to the anal verge [1]. It affects all age groups but is most commonly seen in young and healthy adults with an equal incidence across both sexes. An anal fissure characteristically presents with pain, bright red bleeding per rectum, mucous discharge and constipation. Anal fissures occur predominantly in midline with 90% being located posteriorly and 10% anteriorly. A chronic fissure is characterized by presence for more than 6 weeks, digital rectal examination typically reveals a fissure with indurated margins, fibrosis in base, with or without exposure of horizontal fibres of internal anal sphincter and sentinel tag. There is evidence that anal fissure is associated with spasm of internal anal sphincter (except in postpartum patients) and reduction in blood flow that leads to delayed or non-healing of the ulcer [2-4]. The aim of the treatment is to improve the blood supply of the ischaemic area to facilitate healing, if necessary by reducing resting anal pressure.

Major breakthrough in the management of chronic anal fissure dates back to 1951 when Eisenhammer described internal

sphincterotomy and Parks described open lateral subcutaneous anal sphincterotomy in 1967. In 1969, Notaras further simplified open sphincterotomy to closed lateral anal sphincterotomy. In both these techniques the lower one third to one half of the internal sphincter is divided to lower the resting pressure without destroying the effect of the sphincter. However there is always inherent risk of incontinence associated with these surgical procedures.

Medical management of fissure in ano involves using an agent that produces relaxation of internal sphincter and is known as "chemical sphincterotomy". Nitric oxide (NO) either exogenous or endogenous is one of the most important non adrenergic non cholinergic neurotransmitter mediating relaxation of the internal anal sphincter [5]. Isosorbide dinitrate as a nitric oxide donor has been tried to produce chemical sphincterotomy but it causes headache as a prominent side effect. Nitroglycerine and glyceryl trinitrate is also NO donor which causes relaxation of internal anal sphincter and increases blood flow to allow the fissure to heal in up to two third of the patients [6]. Loder et al. in 1994, demonstrated that topical application of 0.2% glyceryl trinitrate led to decreased resting anal

pressure and was found to be quite effective in relieving symptoms and promoting healing [7]. As cytoplasmic calcium is an important agent for smooth muscle contraction, various calcium channel blocker agents have been used in oral and topical formulations to achieve healing to variable extent in various studies [8,9]. The present prospective study was designed to evaluate and compare effectiveness of topical 0.2% glyceryl trinitrate (GTN) ointment vs lateral internal sphincterotomy (LIS) in the treatment of patients with chronic anal fissure.

## Material and Methods

The present study included a total of 50 patients presented with chronic anal fissure divided into two groups by computer generated randomization. Group A included 25 patients with chronic anal fissure treated with local glyceryl trinitrate ointment 0.2% (liposomal base) applied twice daily for 6 weeks. Group B included 25 patients managed by lateral internal sphincterotomy. All patients were treated by the same surgeon using a uniform method in the lithotomy position with the same technique of sphincterotomy.

## Inclusion criteria

1. Patient willing to give written informed consent.
2. All the cases of anal fissure of more than 6 week duration.
3. Anal fissure with associated features of chronicity like sentinel pile or hypertrophied papillae or exposure of horizontal fibres of internal sphincter.

Patients on medication containing nitrate compound for medical condition, like Ischemic heart disease, pregnant women, anal fissure with inflammatory bowel disease like ulcerative colitis & Crohn's disease, immune-compromise state like human immuno deficiency virus, tuberculosis were excluded. The intensity of pain during defecation was assessed by using Visual Analogue Scale (VAS). This visual analogue was a 10 cm line on which '0' represented no pain and 10 the most severe pain.

All patients in both groups were encouraged for high fibre diet and stool softener. During the course of treatment patients were followed initially twice a week and then at the end of 3 weeks and 6 weeks. At each visit they were examined for symptomatic relief of pain (VAS), healing of fissure, side effect or complication of the treatment, if any. On complete healing of fissure, the patients were asked to stop application of ointment and continue high fibre diet. The healed fissures were then subsequently followed up at 3 months for recurrence, if any. The time required for symptomatic relief and complete healing of fissure was recorded in each case. Patients who did not show any improvement at 6 weeks treated by glyceryl trinitrate ointment were offered the opportunity to undergo a lateral internal sphincterotomy. At the end of the study the data was collected and analysed statistically. The qualitative data presented in the form of numbered percentage. Chi-square test was used as a test of significance for qualitative data in terms of pain reduction and time taken for healing. Student t-test was used as a test of significance for quantitative data. A p value of < 0.05 was considered for significance.

## Observations

All 50 patients in both the groups were followed-up at twice weekly during first week and thereafter at 3 and 6 weeks to find the relief of pain on visual analog scale, fissure healing, side effects of the treatment, if any. The healed fissures were then subsequently followed up at 3 months to see any recurrence.

The mean age in group A was  $34.6 \pm 12.8$  years (18-65) and in Group B  $32.12 \pm 11.57$  (19- 63) years and was comparable. In group A, 19 were male and 6 females vs 20 males and 5 females in group B ( $p > .05$ ). The mean duration of symptoms in group A was  $16.64 \pm 12.31$  weeks whereas in group B was  $16.08 \pm 11.9$  ( $P > .05$ ). Both groups were comparable regarding mean pain score during defecation before treatment- group A  $8.64 \pm 0.95$  vs  $8.44 \pm 1.19$  in group B ( $p > .05$ ). Bleeding during defecation was present in 80% of group A and 72% of group B patients whereas constipation was present in 16 out of 25 (64%) patients in group A and 19 out of 25 (76%) patients in group B. In group A 22 (88%) patients had fissure in posterior midline and 3 (12%) had anterior midline fissure whereas in group B 25 out of 25 (100%) had fissure in posterior midline. In group A 14 out of 25 (56%) patients had anal tag where as in group B 13 of 25 (52%) patients had anal tag.

## Pain relief after treatment

In group A (GTN ointment) mean pain score at the first follow up was  $8.40 \pm 1.19$  on VAS. On subsequent follow ups at the end of 1<sup>st</sup> week, 3<sup>rd</sup> week and 6<sup>th</sup> week the mean pain score was  $7.56 \pm 1.60$ ;  $3.00 \pm 2.25$  and  $1.64 \pm 2.43$  respectively. For group B (lateral internal sphincterotomy) the mean pain score at first follow up (at 72 hrs) was  $3.68 \pm 1.06$ . On subsequent follow ups at the end of 1<sup>st</sup> week, 3<sup>rd</sup> week and end of 6 weeks mean pain score was  $1.40 \pm 1.55$ ;  $0.52 \pm 1.12$ ;  $0.24 \pm 1.20$  respectively. Although patients in both groups had perceptible pain relief as compared to pretreatment levels at 6 weeks of therapy but the decrease in mean pain score in group B (surgically treated) as compared to group A (chemical sphincterotomy) at the end of 6<sup>th</sup> weeks was statistically significant ( $p < 0.05$ ). However complete relief of pain was observed in 16 out of 25 patients after treatment with 0.2% GTN ointment whereas 24 out of 25 patients had complete relief of pain after treatment with lateral internal sphincterotomy (group B) at the end of six weeks of treatment. Therefore number of patients who had complete relief of pain after surgical treatment was statistically significant as compared to patients who were medically treated with 0.2% GTN ointment.

## Healing

None of the patient in either group had complete healing at the end of 1<sup>st</sup> week. However at the end of 3<sup>rd</sup> week 8 patients in group A and 24 patients in group B had completely healed fissures. Complete healing was observed in 18 out of 25 (72%) patients in group A (GTN ointment) whereas all 25 (100%) patients in group B (lateral internal sphincterotomy) had completely healed fissures at the end of six weeks ( $p < 0.05$ ).

## Side effect/complication of the treatment

Except headache which was reported in 9 out of 25 (36%) patients

**Table 1:** Comparison of previous studies with present study with respect to relief of pain.

| Sr. No. | Author                                 | Year | No | Duration | GTN (0.2%) | LIS   | p value                 |
|---------|--|------|----|----------|------------|-------|-------------------------|
| 1.      | Mishra R et al., <sup>12</sup>         | 2005 | 40 | 6 weeks  | 90%        | 90%   | <b>p&gt;0.05</b>        |
| 2.      | Siddique MI et al., <sup>10</sup>      | 2008 | 70 | 6 weeks  | 45.27%     | 100%  | <b>0.001</b>            |
| 3.      | Leo T et al., <sup>13</sup>            | 2011 | 90 | 6 weeks  | 86.6%      | 96.6% | <b>0.161</b>            |
| 4.      | Muhammad I Aslam et al., <sup>11</sup> | 2014 | 60 | 6 weeks  | 56.66%     | 96%   | <b>0.0001</b>           |
| 5.      | Present study                          | 2015 | 50 | 6 weeks  | 72%        | 96%   | <b>0.004 (&lt;0.05)</b> |

**Table 2:** Comparison of previous studies with present study with respect to fissure healing.

| Sr. No. | Author                                 | Year | No. | Duration              | GTN (0.2%) | LIS    | p value       |
|---------|--|------|-----|-----------------------|------------|--------|---------------|
| 1.      | Mishra R et al., <sup>12</sup>         | 2005 | 40  | 6 <sup>th</sup> weeks | 90%        | 85%    | p 0.239       |
| 1.      | Siddique MI et al., <sup>10</sup>      | 2008 | 70  | 6 weeks               | 35.48%     | 84.85% | 0.001         |
| 2.      | Leo T et al., <sup>13</sup>            | 2011 | 90  | 6 weeks               | 53.3%      | 86.7%  | 0.004         |
| 3.      | Muhammad I Aslam et al., <sup>11</sup> | 2014 | 60  | 6 weeks               | 50%        | 92%    | 0.0001        |
| 5.      | Present study                          | 2015 | 50  | 6 weeks               | 72%        | 96%    | 0.004 (<0.05) |

in group A no other side effect was seen in this group. None of the patient in group A had to stop medication due to side effects, whereas only 1 out of 25(4%) patients in group B had a minor haematoma in the perianal area, which was relieved with conservative treatment within 1 week. None of the patients treated surgically suffered from any temporary or permanent incontinence.

## Recurrence

Only 18 patients in group A had healed fissure at the end of 6 weeks. So recurrence was observed in these patients only. Two of these 18 (11.1%) patients had recurrence of the fissure at the same site at 3<sup>rd</sup> month follow up. All 25 patients in group B had healed fissure at the end of six weeks. However at the end of 3 months 2 patients of this group had recurrence. However, there was no statistically significant difference in the frequency of recurrence between the two groups (p=0.729).

## Discussion

Both groups in study were comparable regarding age and sex. The most common symptoms were pain during defecation, bleeding per rectum and constipation. More than two third of patients in group A and all patients in group B presented with posterior midline fissure.

During the course of present study the mean pain score decreased from 8.64 (at presentation VAS score) to 1.64 after application of GTN ointment and 8.44 to 0.24 after lateral internal sphincterotomy at the end of six weeks. Although patients in both groups had perceptible pain relief but the decrease in mean pain score in group B as compared to group A was statistically significant (p=0.049) at the end of six weeks of treatment. At the end of six weeks treatment 24 out of 25 (96%) patients had complete pain relief after treatment with lateral internal sphincterotomy and 16 out of 25 (64%) patients had complete pain relief after treatment with 0.2% GTN ointment (p<0.05). The results of present study are in confirmity with others who also observed similar pain relief and in variance with few others

because of variable observations in literature concerned with this particular disease [10-13]. (Table 1).

In the present study complete healing of fissure was observed in 18 out of 25 (72%) patients in group A and all 25 patients (100%) in group B at the end of six weeks of treatment (p<0.05). The result of the present study are in confirmity with the study conducted by Siddique et al. who found 28 out of 33 (84.85%) patients after treatment with lateral internal sphincterotomy and 11 out of 31 (35.48%) patients after treatment with GTN ointment (p<0.001) had complete healing at the end of six weeks [11]. The result of the present study are in variance with the results of a study undertaken by Mishra et al., on 40 patients of chronic anal fissure who found that 18 out of 20 patients healed after treatment with 0.2% GTN ointment and 17 out of 20 patients healed after treatment with lateral internal sphincterotomy at the end of 6<sup>th</sup> weeks of treatment [12] (Table 2).

In the present study headache was the only side effect observed with the application of GTN ointment (group A) during the course of treatment. Nine out of 25 patients treated with 0.2% GTN ointment reported headache as the major side effect. None of the patients in group A treated with GTN ointment had to stop medication due to side effect. Whereas in group B patients treated with lateral internal sphincterotomy only 1 case of haematoma was observed. No other complication was observed in either group. The results of the present study are in confirmity with the results of study undertaken by Mishra R et al., who found that 5 out of 20(25%) patients had experienced either a local burning sensation or mild headache after treatment with 0.2% GTN ointment [12]. Whereas 12 out of 20 patients(60%) experienced either mild bleeding on first postoperative day or haematoma, wound infection or a perineal abscess after treatment with lateral internal sphincterotomy (p=0.025). Siddique et al., in their study on chronic anal fissure found that 2 out of 33 patients (6%) after treatment with lateral internal sphincterotomy had minor incontinence to flatus on stress whereas during the course of treatment with 0.2% GTN ointment 8 out of 31(25.8%) patients experienced mild headache [10]. The results of the present study are also in confirmity with the recent study undertaken by Muhammad et al., who found 20 out of 30(66.6%) patients developed headache after treatment with 0.2% GTN ointment whereas 2 out of 30 (6.6%) patients had incontinence to flatus and feces after treatment with lateral internal sphincterotomy [11]. However the results of the present study are in variance with the study conducted by Leo et al., on 90 patients of chronic anal fissure who found that 6 out of 30 (20%) patients reported headache which was mild degree and relived by simple paracetamol tablet after treatment with 0.2% GTN ointment, whereas only 3 (10%) out of 30 patients showed either flatus incontinence or anal seepage in lateral internal sphincterotomy group (p=0.278) [13].

In the present study patients using GTN ointment (group A) had a 11% recurrence rate while after treatment with lateral internal sphincterotomy (group B) 8% recurrence rate was observed at 3 month follow up (p>0.05). The results of the present study are in confirmity with the study undertaken by Oettle on 24 patients of chronic anal fissure who found that at the end of 24 months follow up none of the patients in either groups (0.2% GTN ointment and lateral

**Table 3:** Comparison of previous studies with present study with respect to recurrence.

| Author                        | Year | No. | Duration  | GTN group | LIS | p value      |
|-------------------------------|------|-----|-----------|-----------|-----|--------------|
| Oettle GJ <sup>14</sup>       | 1997 | 24  | 24 months | 0         | 0   | 0            |
| Ellaban et al., <sup>15</sup> | 2010 | 80  | 12 weeks  | 2.5%      | 0   | <b>0.281</b> |
| Leo T et al., <sup>12</sup>   | 2011 | 90  | 12 weeks  | 0         | 0   | 0            |
| Present study                 | 2015 | 50  | 12 weeks  | 11%       | 8%  | <b>0.729</b> |

internal sphincterotomy) who had healed fissure had any recurrence [14]. Various other authors have also reported similar results in comparative studies [12,15]. (Table 3).

## Conclusion

Although topical application of 0.2% GTN ointment for chronic anal fissure is safe and a high rate of healing of fissure can be achieved without risk of incontinence, but symptomatic relief of pain occurs at a slower rate than lateral sphincterotomy. It may be considered as a satisfactory first line option in the treatment of chronic anal fissure. However lateral internal sphincterotomy remain effective and may be considered as the treatment of choice in chronic anal fissure when the procedure is performed by an experienced and skilled surgeon.

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