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Nitroglycerine: A Paradigm in Treatment of Chronic Anal Fissure

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Abstract

Background/ Aims: Anal fissure is a common problem that causes significant morbidity in a young population. Surgical techniques like manual anal dilatation or lateral internal sphincterotomy, effectively heals most fissures but may result in anal continence. 'Chemical Sphincterotomy' is thus investigated and used as the possible first line treatment for anal fissures. The present study is designed to evaluate the role of topical Nitroglycerine ointment in cases of chronic anal fissures.

Methods: A prospective observational study was conducted at a tertiary healthcare centre. A total of 90 patients of chronic anal fissure were included in the study. Nitroglycerine ointment (0.2%) application was advised to all patients (thrice daily). Lateral internal sphincterotomy was performed where medical management failed or in cases with severe pain. Follow up was maintained for a period of 6 weeks or until fissure is healed.

Results: Out of the total 90 cases, 34 (37.7%) cases responded to Nitroglycerine ointment while 56 (62.3%) required lateral internal sphincterotomy. The relief of pain was faster with sphincterotomy than with Nitroglycerine, as observed by comparing mean pain score at the end of 6 weeks (0.51 vs 1.33; $p<0.01$). Wound infection rate for sphincterotomy was 3.6%.

Conclusion: Nitroglycerine ointment is effective in about a third of the chronic anal fissures cases. Thus it should be advocated as the first option of treatment for chronic cases and sphincterotomy should be reserved for patients with therapeutic failure of pharmacological treatment and those with severe pain.

Keywords: Chronic Anal Fissure; Chemical Sphincterotomy; Lateral Internal Sphincterotomy; Nitroglycerine; Muco-Cutaneous

Abbreviations: NTG: Nitro-glycerine

Introduction

Anal fissure is a distinct clinic-pathological condition of the lower anal canal and is the most common cause of severe anal pain [1]. Anal fissure is a common problem that causes significant morbidity in a young and otherwise healthy population. It may extend from the muco-cutaneous junction to the dentate line and is maintained by the contraction of the internal anal sphincter. It can be acute or chronic. An acute anal fissure has the appearance of a clean longitudinal tear in the anoderm, with little surrounding inflammation. A chronic fissure is usually deeper and generally has exposed internal sphincter fibres in its base. It is frequently associated with a hypertrophic anal papilla at its upper aspect and with an irritated skin or sentinel pile at its distal aspect.

There has been a lot of progress in the understanding of the anatomy of the anal canal and the mechanism of continence of rectum and anal canal. This has enabled the surgeon to deal with the fissure, keeping the spastic anorectal ring intact, without interfering with continence and eradicating the disease. Surgical techniques like manual anal dilatation or lateral internal sphincterotomy, effectively heals most fissures within a few weeks, but may result in permanently impaired anal continence. This has led to the research for alternative non-surgical treatment, and thus 'Chemical Sphincterotomy' is being investigated and used as the possible first line of treatment even for chronic anal fissure [2].

Topical Nitro-glycerine (NTG) ointment has been shown to be effective but has reduced compliance due to headache as side effect [3]. Topical calcium channel blockers offer a suitable alternative for fissure treatment, healing 65-95 % cases with lesser side effects. Botulinum toxin injections are also used.

The present study was designed to evaluate the role of topical Nitroglycerine ointment in chronic anal fissures, its effectiveness with reference to pain relief, fissure healing and its side effect. We also studied the failure rate of topical Nitroglycerine ointment and requirement of surgical intervention.

Material & Methods

A prospective observational study was conducted at a tertiary healthcare centre. Study was commenced after taking approval of Institutional Ethical Committee.

Inclusion Criteria

All consenting patients of chronic fissure in ano situated in midline anteriorly or posteriorly or both were selected.

Exclusion Criteria

1. Acute anal fissures
2. Fissure in ano situated other than midline
3. Patients with tuberculosis, Crohns disease, AIDS
4. Associated with abscess, haemorrhoids or fistula

Methodology

A total of 90 patients of chronic anal fissure were included in the study by consecutive type of non-probability sampling. Informed consent was taken from all subjects by the principal investigator. Patients were clinically examined and a pre-formed proforma was filled.

A single brand of Nitroglycerine ointment (Nitrogesic) 0.2% was used. The dose of administration was based upon length of ointment applied. A length of 2 cm as measured by a small custom made measuring device provided by the manufacturer of the proprietary preparation. The frequency of application was advised to be thrice daily. Stool softeners, sitz bath and high fibre diet were started. In case of patient complaining of headache, dose adjustment and frequency of application was suitably adjusted. In cases where patient complained of headache, the following measures were adopted. The patient was advised to apply the ointment over the fissure twice daily using a gloved finger. Also, tablet Paracetamol 500 mg was administered for symptomatic treatment for headache. Patients in which medical management failed were posted for lateral internal sphincterotomy. The patients were followed up for a period of 6 weeks or until fissure is healed and were evaluated for relief of symptoms by comparing VAS score.

Data Analysis

Data was analyzed using SPSS 21.0 (SPSS Inc., Chicago, IL, USA) using appropriate statistical tests.

Results

The commonest age group affected was 20-30 years age group (48.9%) and least affected was 51-60 years age group (4.4%).

Age Distribution	N	%
20-Nov	9	10.00%
21-30	44	48.90%
31-40	20	22.20%
41-50	13	14.40%
51-60	4	4.40%
Total	90	100.00%

Table 1: Distribution of subjects based on Age group.

Most common presenting complaints were pain, bleeding PR and constipation. On Per rectal examination, there was sphincter spasm noted in all patients. On per rectal examination, sentinel tag was present in all cases. The location of fissure was posterior in all male patients and majority of female patients. Out of total 90 cases, 34 (37.7%) cases responded to Nitroglycerine ointment while 56 (62.3%) required lateral internal sphincterotomy (Table 2).

Response to NTG	N	%
No	56	62.20%
Yes	34	37.80%
Total	90	100.00%

Table 2: Distribution of subjects based on Response to NTG.

Fissure was completely healed in 30 (33.3%) cases between 6-8 weeks, 3 patients required 8-10 weeks while 1 required 10-12 weeks to heal. A total of 20 (22.2%) were almost free from pain while 14 (15.6%) had slight pain on follow up at the end of 6 weeks (Table 3 & Table 4). The 56 (62.3%) patients who were not healed by NTG, required lateral internal sphincterotomy. The healing of fissure was achieved in < 8 weeks in all these cases.

Healing	N	%
6-8 weeks	30	33.30%
8-10 weeks	3	3.30%
10-12 weeks	1	1.10%
Not healed	56	62.20%
Total	90	100.00%

Table 3: Distribution of subjects based on assessment of healing.

Pain	N	%
No pain	20	22.20%
Slight Pain	14	15.60%
Severe Pain	56	62.20%
Total	90	100.00%

Table 4: Distribution of subjects based on Subjective Pain assessment.

Remaining 56 (62.2%) were not relieved of pain and underwent lateral internal sphincterotomy. Of the 90 patients, 19 patients (21.1%) complained of headache. In all the 56 patients who underwent lateral internal sphincterotomy, fissure was completely healed between 4-6 weeks and all of them were free of pain. Incontinence and fistula/ abscess was not seen in any case in our study. Two patient (3.6%) had wound infection which resolved with antibiotics, daily cleaning and dressing. The relief of pain was faster with lateral internal sphincterotomy than with NTG application as observed on comparison of mean pain score at the end of 6 weeks (0.51 vs 1.33; $p<0.01$) (Table 5).

	Group	N	Mean (SD)	p-value
VAS Score (6 weeks)	**NTG**	34	1.33 (0.19)	**<0.05**
	Lateral internal sphincterotomy	56	0.51 (0.05)	

Table 5: Comparison of mean VAS Score at 6 weeks.

The patients who had complete healing of fissures in both the treatment arms were observed for recurrence in the subsequent visit till 6 months. It was observed that complete healing was not followed by recurrence in both treatment arms.

Discussion

The treatment of anal fissure aims at reducing internal anal sphincter tone. Lateral internal sphincterotomy is the current gold standard for the treatment of chronic anal fissures. It involves partial division of the internal anal sphincter away from the fissure. Topical Nitroglycerine have been shown to lower resting anal pressure and promote fissure healing and chemical sphincterotomy is now the first line of treatment for acute as well as chronic anal fissures in many centres [4]. The present study thus attempted to analyse the role of Nitroglycerine in the Indian setting for the treatment of chronic anal fissures.

In this study, the commonest age group affected was 20-30 years age group (48.9%) and least affected were 51-60 years age group (4.4%). According to Goligher, et al. the disease is usually encountered in young or middle aged adults [5]. In Udwadia TE series, maximum incidence was seen in 31-40 years age group [6]. The incidence was maximum in the age of 30 to 40 years in a study by Sharma, et al. [7]. We observed a higher incidence of fissure in males with male to female ratio as 1.57: 1 in present study. The study by Sharma, et al. also showed male preponderance with male to female ratio of 1.2:1. [7]. Although the sex distribution is equal in case of anal fissure, as supported by many other studies,the results of our study which showed male preponderance, was may be due to various social factors prevalent in our society which leads to under-reporting of the symptoms in case of females [5,8,9].

The clinical findings, which showed that painful defecation and bleeding per rectum were most common complaints, was supported by study of Morgan, et al. Various other literature also supported that constipation and anal spasms were the next most common clinical features [10-13].

In this study posterior midline fissure (96.7%) was more common than anterior (3.3%) midline fissure. Our results are comparable with the study by Boulous, et al. which says that posterior fissure (85.7%) is more common than anterior fissure (14.2%) [14].

Out of 90 patients undergoing treatment with Nitroglycerine ointment, 34 healed completely (37.8%). The average duration of healing was 6-8 weeks. A total of 20 (22.2%) patients were almost free from pain while 14 (15.6%) had slight pain on follow up at the end of 6 weeks. Of the 90 patients, 19 patients (21.1%) complained of headache. Fifty six (62.2%) of chronic fissures who did not heal or who had severe pain after 6 weeks of NTG therapy underwent lateral internal sphincterotomy. In all of these 56 patients (100%), fissure was completely healed between 4-6 weeks and all of them were free of pain. Two cases in sphincterotomy group had wound infection while no other complications were reported in these patients. The relief of pain was faster with sphincterotomy than with NTG application as observed on comparison of mean pain score at the end of 6 weeks (0.51 vs 1.33; $p<0.01$).

Manookian CM, et al. studied 81 patients of acute/ chronic anal fissure and observed healing rate with GTN in chronic fissure as 54% [15]. Similarly Bacher, et al. observed healing rate as 12.5% in chronic fissures [16]. Mishra R, et al. compared GTN and lateral sphincterotomy for chronic anal fissures [17]. Sphincterotomy relieved pain much earlier compared to GTN (70% vs 40% at 2 weeks, $P = 0.0032$); but after 4 weeks of treatment, pain relief in both groups was comparable. Healing in the sphincterotomy group was also earlier than with GTN (55% vs 0% at 2 weeks, $P < 0.0001$; and 85% vs 30% at 4 weeks, $P < 0.0001$); but after 6 weeks, healing in both groups was comparable.

In another similar study by Aslam M, et al., 15 patients (50%) of chronic anal fissure were successfully treated by GTN while 28 (93%) patients with lateral internal sphincterotomy were successfully treated [18]. Two patients (6.6%) in lateral sphincterotomy Group suffered from incontinence due to flatus and feces as a complication of the procedure. El-labban, et al. also compared the effectiveness of local glyceryl trinitrate (Group 1) versus internal sphincterotomy (Group 2) in the management of chronic anal fissure [19]. In group 1, healing of fissures occurred in 85% of patients after 8 weeks therapy. Headache as a side effect developed in 65% of patients. In group 2, healing occurred in 97.5% of patients after 8 weeks. Incontinence to flatus occurred in 3 patients (7.5%), mild soiling in 2 patients (5%), and one patient developed wound infection.

Observations from all these studies supports that Topical GTN should be the initial treatment in chronic anal fissure while internal sphincterotomy should be reserved for patients who did not respond to GTN therapy and those with severe pain (as healing is faster with sphincterotomy).

Conclusion

Nitroglycerine ointment has a definitive role in chronic fissures. Lateral internal sphincterotomy though is the current standard treatment for chronic fissures, exposes patients to risks of surgery and anaestheisa and other complications like incontinence. In present study Topical GTN was effective in one third cases of chronic fissure with respect to both symptom relief (pain, bleeding) and fissure healing. In contrast with surgery, chemical sphincterotomy with Nitroglycerine is reversible and therefore unlikely to have adverse effects on continence. Thus, Topical Nitroglycerine should be advocated as the first option of treatment for chronic anal fissures while sphincterotomy should be reserved for patients with

therapeutic failure of pharmacological treatment and those with severe pain.

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