ORIGINAL ARTICLE

EFFICACY AND SAFETY OF GLYCERYL TRINITRATE (GTN) IN THE TREATMENT OF CHRONIC ANAL FISSURE

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ABSTRACT

Background: Anal fissure is a commonly distressing disease. The objective of the study was to determine clinical presentation and efficacy of Glyceryl trinitrate (GTN) in chronic anal fissure.

Material & Methods: It is a descriptive study that was conducted in the department of surgery District Headquarter Teaching Hospital D.I.Khan from January 2015 to August 2015. A total of 60 consecutive patients with chronic anal fissure were selected. Demographic variables were gender and age. The research variables were painful defecation, bleeding per rectum, duration of symptoms, presence of skin tags and efficacy of GTN. All patients were treated with 0.2% GTN ointment applied three times a day to the anus. These patients were followed at 2 and 6 weeks to assess symptomatic relief and adverse effects. Data was collected on Proforma and was analysed on SPSS version 11.0.

Results: By 14 days of treatment, 8 patients were pain-free, While 30 out of them were pain-free by end of 6 weeks of treatment. Out of 18 patients, who presented with bleeding per rectum (P/R), 14 were still having bleeding P/R by the end of 2 weeks that improved to 6 by the end of 6 weeks. And 8 patients were in severe pain even by end of 6 weeks. None of the patients had to discontinue treatment with GTN due to side effects.

Conclusions: The symptomatic relief occurred at a slower pace in patients receiving topical 0.2% Glyceryl trinitrate ointment. However, it can be used as first-line of treatment in patients who are not fit for surgery.

KEY WORDS: Anal fissure; Nitroglycerin; Nitric oxide.

This article may be cited as: Khitab N, Ahmad N, Hussain A, Aurangzeb M. Efficacy and safety of glyceryl trinitrate (GTN) in the treatment of chronic anal fissure. Gomal J Med Sci 2017;15:161-4.

INTRODUCTION

Anal fissure is a linear tear in the epithelium of the anal canal overlying the internal sphincter. It occurs in all age groups with equal prevalence in both genders.[1] Patients mostly presents with severe pain after defecation & bright red rectal bleeding.[2,3] Fissure can be acute or chronic. Acute fissures have the appearance of a simple tear in the anoderm, while the chronicity of fissures is determined by the presence of symptoms (pain on defecation, bleeding per rectum) lasting for more than six weeks, & along with classical triad of fissure with sentinel skin tag, and hypertrophied anal papilla.[4-6] Fissures are predominantly located in the posterior midline, but 25% of females & 8% of males have anterior fissures. Fissures occurring in lateral positions should raise suspicions for other disease processes e.g.; crohn's disease, tuberculosis, syphilis, aids or anal cancer etc.[3,7] It is generally accepted that chronicity is due to hypertonia of anal canal which results in poor perfusion of anoderm especially in posterior midline that has inherently poor vascular supply.[3,8]

Anal fissure was first described as a disease of rectum by Baron Boyer in 1689. He termed the fissure a disease of rectum, associated with constriction of anus.[9]

About 30 to 40 percent of the population suffer from proctologic pathologies at least once in their lives[10] and anal fissures affect about 10% of them.[11]

Most acute fissures don't require any further

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Date Submitted: 01-03-2017
Date Revised: 18-05-2017
Date Accepted: 21-10-2017

treatment and heal well with conservative treatment with stool softeners, high fibre diet, pain killers & local hygiene.[5,6,11] But chronic fissures usually don't respond to such measures & have traditionally been treated by surgery, either by lateral internal sphincterotomy (LIS), by manual dilatation, fistulectomy &/or sphincterotomy and anal advancement flap.[6-11] A non-surgical method for the treatment of chronic anal fissure includes temporary or medical sphincterotomy, by local application of agents that reduce the sphincter pressure until the fissure has healed.[3,11] The idea of topical sphincterotomy with nitroglycerine(NTG) was first proposed in 1994 after studies by Loder et al[11] & Guillemot et al.[12] They demonstrated decreased resting anal pressure with 0.2% Glyceryl trinitrate ointment. Topical sphincterotomy with calcium channel blocker was introduced in 1999[13] after studies by Chrysos et al & in 2000 with topical diltiazem.[14] A combine surgical and medical approach with the use of botulinum toxin injection into anal sphincter also causes reversible sphincterotomy and was first investigated in 1993.[15-16]

NTG is a nitric oxide donor which causes relaxation of anal sphincter. Local application of 0.2% GTN ointment to the distal anal canal is reported to heal chronic anal fissure in a good number of patients.[17] This results in a reversible improvement and eliminates the risks of permanent anal incontinence associated with surgery in up to 35% of patients.[17]

Surgery has also been associated with a failure rate of less than 6%[18] due to limited sphincterotomy[19-20] which often necessitates further surgery and increased risk of incontinence in otherwise healthy young adults. Due to recurrence and incontinence; non-surgical methods are therefore desirable.

With so many potentially conservative options we investigated the efficacy of GTN in the treatment of chronic anal fissure as it is easily available & no recent work has been done at our institution.

The objective of the study was to determine the demographics, clinical presentation and efficacy of Glyceryl trinitrate (GTN) in chronic anal fissure.

MATERIAL AND METHODS

This descriptive cross-sectional study was conducted in the Department of Surgery, DHQ Teaching Hospital, Dera Ismail Khan from January 2015 - August 2015. Sample size was a total of 60 patients with chronic anal fissure selected on the basis of convenient sampling.

All new patients with chronic anal fissure of, age more than or equal to 16 years, of both gender were included. Patients with a history of more than 2 years and patients with fissures secondary to tuberculosis, crohn' s disease, or malignancy etc were excluded. Also, the pregnant/lactating patients and patients taking any smooth muscle relaxant medications were excluded from the study.

Consent was taken from all the patients. Approval of the study was taken from ethical committee DHQ Teaching Hospital, D.I.Khan. Detailed clinical history, digital rectal examination and proctoscopy (to exclude secondary causes of fissure) were done in all cases. Chronic anal fissure operationally defined as the presence of a linear ulcer in the distal anal canal, indurations and a sentinel skin tag, with the associated symptoms, of painful defecation and bleeding per rectum. The patients were precisely taught at OPD about the standard regimen of using a "pea-sized amount" of 0.2% preparation of Glyceryl trinitrate in the form of ointment, applied with vaginal applicator or gloved finger three times a day (8 am, 12 pm, and 5 pm) for 6 weeks. The patients were followed up at 2nd and 6th week in the surgeon office. The variable of pain was assessed on a visual analogue scale and bleeding by clinical presence and absence. Only those patients with complete disappearance of pain were considered as having successful pain relief. The pain was assessed on 100 mm visual analogue scale (VAS) and bleeding on the clinical basis. Demographic variables were gender (male, female) and age. The research variables were painful defecation (yes, no), bleeding per rectum (yes, no), duration of symptoms (1-3 years, >3 years), presence of skin tags (yes, no) and efficacy of GTN (painful defecation, bleeding per rectum). All the data was recorded on structured Proforma. All variables being categorical except age were analyzed descriptively using SPSS version 11.

RESULTS

Patients of age 16 to 60 years (mean age 34 years), 20 males (33.3%) and 40 females (66.7%). Examination revealed skin tags in 20 patients (33.3%). Regarding clinical presentation 58 out of 60 patients presented with painful defecation which persisted for a variable time after defecation. Patients were found to have been suffering from symptoms of fissure for a period ranging from 1 to 3 years (40 patients).

The clinical efficacy of GTN in terms of pain relief and bleeding per rectum at 2nd and 6 weeks are shown in figure 1 and 2 respectively.

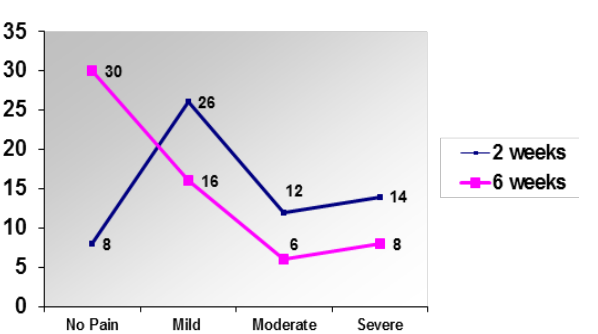

Figure 1: Graph showing the clinical efficacy of GTN in terms of pain relief in 2nd and 6th weeks respectively.

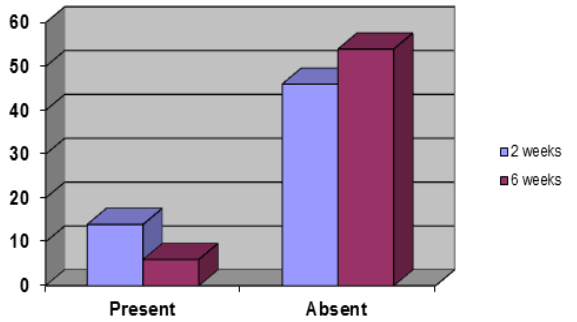

Figure 2: Graph showing clinical efficacy of GTN in term of bleeding per rectum in 2nd and 6th week respectively.

DISCUSSION

Anal fissure is a common painful perianal condition in surgical practice. Raised anal resting pressures caused by hyper tonicity of the internal anal sphincter (IAS) and ischemia of anal canal have been suggested as factors that are important in pathogenesis of anal fissures.[3,8]

The aim of treatment is to reduce anal hypertonia, which may improve anodermal blood flow and heal the fissure. Until approximately 5 years ago, lateral internal sphincterotomy was the gold 'standard' in treatment, producing rapid symptom relief and healing rates of over 90%, but it is now less popular as disturbances incontinence can occur in up to 35% of patients.[3,6]

The recognition of organic nitrates as the non-adrenergic, non-cholinergic neurotransmitters mediating relaxation of the internal anal sphincter has initiated the wide-spread use of organic nitrates in the treatment of chronic anal fissure. These agents are metabolised at a cellular level to release NO which, in turn, mediates relaxation of the internal anal sphincter.[12,20] This study assessed its local use in the form of an ointment in the treatment of chronic anal fissure. Local application of 0.2% Glyceryl trinitrate ointment can improve anodermal blood flow by inducing sphincter relaxation and thereby results in symptomatic relief and healing of fissure without compromising the anal continence.

The apparent benefits of this modality would seem greater for those patients with high risk of surgery-induced complications (like incontinence), including multiparous women, and those with prior anal surgery, recurrent fissures, or perineal radiotherapy. It would also be good for those who are not fit for surgery. Among other benefits, would include a reduction in hospital waiting lists and so on the cost savings for a condition previously requiring surgery. But there are no data available on its safety in lactating mothers.

The strength of our study is that it is the first study of reasonable good sample size at our institution. The weakness of our study is that it is not a randomised control trial, comparing GTN with surgical methods and we don't have other modalities to compare with it. Although literature has found GTN a very effective modality in the management of acute fissures, but its efficacy in terms of chronic anal fissure shows a healing rate of up to 90 percent.[11]

Although there have been few studies, which showed better results with a high concentration of GTN but the safety remains questionable due to the high rate of complications. Whilst there is little difference in the overall outcome of treatment with the use of higher doses (57% with 0.4% vs. 36% with 0.2%).[22] This benefit, however, occurs at the expense of more headaches and a lower compliance rate. Some authors reported that anal fissure treated with topical 0.3% nitroglycerin ointment applied to the anoderm three times per day was only effective in approximately one-half of patients with an acute anal fissure and 41% in chronic anal fissure. Even when effective, 75% of patients reported an adverse reaction Despite effectiveness, 75% of patients reported an adverse reaction in the form of headache. This study had a much higher incidence of adverse reactions than our study and we think that this is attributable to the higher concentration (0.3% GTN) than ours (0.2% GTN).[21,23]

However, there are studies which describe inefficacy of 0.2% GTN in patients with chronic anal fissure in terms of symptomatic relief, which is in accordance with our study that also showed inadequate pain relief in most of the patients and only 8 out of 60 patients were pain free at 2 weeks & 30 patients at 6 weeks. While 8 patients were in severe pain even at the end of 6 weeks of treatment & this finding is consistent with the studies which claim failure of GTN ointment in the treatment of chronic anal fissure.[22,24]

According to various studies this is actually very prolonged history and the presence of sentinel pile which made them an unsuitable candidate for pharmacological therapy.[24] The majority of the patients in our study presented with a history of more than one year and 3 of our patients had this problem for 10 years or more.

A headache is the chief side effect noticed by patients using topical GTN ointment. According to various studies frequency of a headache varies from 19% to 44%. In our study one-quarter of the patients had a mild headache, which didn't need any treatment. Anal burning and soiling have been reported in various studies, which were not seen in our cases.

This study revealed that the symptomatic relief occurred at a slower pace in patients receiving topical 0.2% Glyceryl trinitrate ointment. Because it was a short-term study, no conclusions can be drawn about long-term results with this treatment modality. And in this study, we don't have any comparison group. And we also have noticed that the GTN was least effective in patients with very prolonged history, so there

is need have further research on this un-answered question. Moreover, large sample size randomised control trial comparing GTN with LIS may be carried out in future.

CONCLUSION

The symptomatic relief occurred at a slower pace in patients receiving topical 0.2% Glyceryl trinitrate ointment in patients with chronic anal fissure. However, it can be used as first-line of treatment in patients who are not fit for surgery.

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CONFLICT OF INTEREST
Authors declare no conflict of interest.
GRANT SUPPORT AND FINANCIAL DISCLOSURE
None declared.

AUTHORS' CONTRIBUTION

Conception and Design:	NK,
Data collection, analysis & interpretation:	NK, NA, AH
Manuscript writing:	NK, MA