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Effectiveness and Complications of 0.2% Glyceryl Trinitrate in the Treatment of Chronic Anal Fissure

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Summary:

Background: ***The aim of this study was to analyze the effectiveness and morbidity of chemical sphincterotomy by 0.2% glyceryl trinitrate (GTN) in the treatment of chronic anal fissure. The main end points were symptom relief, fissure healing and side effects.***

Methods: ***A prospective study was conducted to see the effectiveness and side effects of 0.2% glyceryl trinitrate in the treatment of patients with chronic anal fissure attending the outpatient department of surgery from February 2004 to the end of February 2005. All the patients were followed up at 2 weeks interval for 8 weeks. The primary focus was fissure healing and the secondary focus were on improvement of symptoms, need for surgical sphincterotomy and side effects.***

Results: ***One hundred and twenty two adult patients, both male and female with chronic anal fissure were treated with local application of 0.2% glyceryl trinitrate. Pain relief occurred earlier than fissure healing. At the end of 8 weeks treatment about two third of the total patients got complete pain relief and fissure healing. Headache was the major side effect.***

Conclusion: ***Topical application of 0.2% glyceryl trinitrate (GTN) should be the initial treatment of choice for chronic anal fissure to avoid the long term complication of incontinence following surgical sphincterotomy.***

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Introduction:

Anal fissure is a linear tear in the anoderm below the level of the dentate line. The site of election for an anal fissure is midline posteriorly (90% overall). The next most frequent is midline anteriorly.[1] It is responsible for significant morbidity causing pain and bleeding during defaecation in all age groups but usually in young adults. The pain is often severe, tearing in nature lasting for minutes or for hours. In about 50% cases itching may accompany anal fissure. Most anal fissure are acute and settle spontaneously or with stool softening laxatives. Chronic fissures are those failing to heal within 6 weeks and usually need further intervention to heal.[2] The exact aetiology of primary anal fissure is unknown. Tear in the anoderm results from forceful dilatation of the anal canal, commonly during defaecation. The anoderm is disrupted, exposing the underlying internal sphincter muscle. Eventually the muscle goes into spasm and fails to relax with next bowel movement. This leads to further tearing, deepening of fissure and increased muscle irritation and spasm. The persistent muscle spasm leads to relative ischaemia of the overlying anoderm and inhibits healing.[3] Another theory is based around the severe internal sphincter spasm which predates fissure formation and the paucity of blood supply in the midline posteriorly.[4] This combination may lead to ischaemia. The main underlying pathology, however appears to be a high resting anal pressure caused by increased sphincter tone. The blood supply of the anal canal has to pass through the internal sphincter and therefore spasm of this muscle reduces the blood flow and oxygen tension in the skin of the anal canal.[5] Diagnosis of primary or idiopathic chronic anal fissure is made mostly from history and a gentle rectal examination. Usually a skin tag overlying the fissure and the fissure itself can be seen everting the anal canal using lateral traction. The basic principle of treating anal fissure is to reduce the internal anal sphincter tone. Reduction in anal pressure in chronic anal fissure has been shown to increase anodermal blood flow with

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resultant pain relief and early healing.[6,7,8] In patients with minimal symptoms or with shorter duration this may be achieved by topical application of local anaesthetics or bulk laxatives. Patients with more severe symptoms require further intervention. Lateral internal sphincterotomy is said to be successful in about 95% of cases.[5] But this method is associated with disturbance of faecal continence in a significant proportion of patients.[9] In reducing the anal tone anal stretching is attractive to some surgeons because of its extreme simplicity; But this technique is liable to produce an uncontrolled tear of the sphincter and is associated with severe complications including bleeding, perianal bruising, strangulation of associated prolapsed piles, perianal infection, fourniers gangrene and full thickness rectal prolapse. Bacteraemia occurs in upto 8% of patients.[9] To avoid these unacceptable complications, different pharmacological agents are being in use for topical application in order to relax internal sphincter (Chemical sphincterotomy) causing a reduction in resting anal tone with secondary increase in anal blood flow with eventual healing of chronic anal fissure in a significant number of patients within 6-8 weeks time. Much work has gone into the development of new pharmacological agents like glyceryl trinitrate, botulinum toxin, diltiazem, nifidipine that can promote healing of chronic anal fissure by producing reversible chemical sphincterotomy.[10] Nitric oxide is the neurotransmitter involved in mediating the relaxation of internal sphincter. The first chemicals successfully used to treat chronic anal fissure were nitric acid donors – GTN ointment and isosorbide dinitrate. A pea-sized amount of 0.2% GTN ointment applied twice or thrice a day to the anal canal for 8 weeks heals upto two thirds of chronic anal fissures.[7]

Methods:

The study was designed as a prospective study after approval from the department of surgery, BSMMU, Dhaka. A total of 122 adult patients, both male and female, over the age of 18 years with chronic anal fissure attending the outpatients department of Bangabandhu Sheikh Mujib Medical University Hospital since February 2004 to the end of February 2005 were included in this study. There was no drop out. Chronicity was defined as features lasting for more than 6 weeks, indurations of fissures, visible sphincter fibres at the base of the fissure and a sentinel piles. Patients with secondary fissures, diabetes mellitus, pregnancy and fissures complicated with fistula and anal stenosis were excluded from the series. The patients were asked to apply 0.2% GTN ointment to the distal anal canal twice daily for 8 weeks. They were followed up at 2 weeks intervals for 8 weeks for pain relief, healing of fissure, compliance and for any side effect. They were advised supportive measures like sitz baths and stool softening agents with high fibre diet. The primary endpoint was fissure healing and secondary endpoints were symptom relief, need for surgical sphincterotomy and side effects. Pain relief was defined as complete absence of pain. Healing of fissure was accepted when full epithelialization occurred over fissure.

Results:

A total of one hundred and twenty two adult patients, both male and female were included in this study. Majority of the patients were in the 3rd and 4th decade of life (Table 1). Painful per rectal bleeding, anorectal pain and postdefaecation burning and itching with mucus discharge were the presenting features with a variable duration ranging from 6 weeks to more than one year. Following application of 0.2% GTN 17 patients (13.93%) were pain free after two weeks (Figure 1). None had a healed fissure during this period. At four weeks of treatment 37 patients (30.33%) became symptom free with fissure healing in 27 patients (22.15%). After 6 weeks treatment more patients became symptom free with healed fissures numbering to 59(48.36%) and 49(40.16%) respectively. Finally at the end of 8 weeks treatment 95 patients (77.86%) became symptom free and 82 patients (67.2%) had complete healing of fissure. Rest of the patients did not experience significant symptom relief or healing of fissure and were advised for surgical sphincterotomy. During the topical application of 0.2% GTN 39 patients (31.96%) had experienced mild headache persisting for an average of 4 days, but none of them discontinued the treatment because of prior counselling (Figure II). 22 patients (18.03%) had mild anal burning and minor incontinence to flatus and mucus occurred in 6 patients (4.9%).

Table-I

Age and Sex distribution of patients (n=122)

Age range (in years)	No. of patients		Total	Percentage (%)
	Male	Female		
11-20	10	04	14	11.47
21-30	19	16	35	28.68
31-40	22	27	49	40.16
41-50	08	05	13	10.65
51-60	02	06	08	06.55
>60	02	01	03	02.45

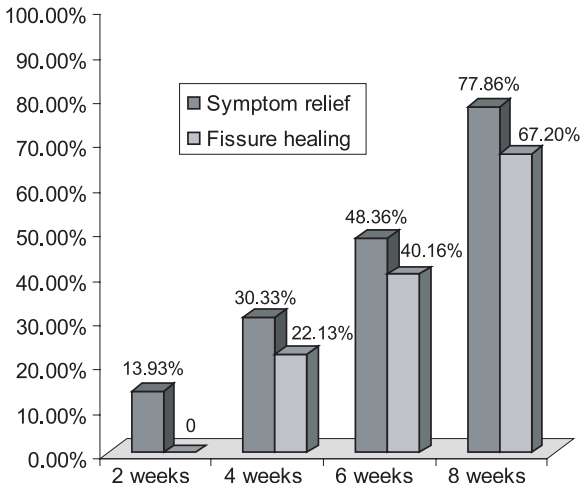

Fig.-1: *Result of treatment (n=122)*

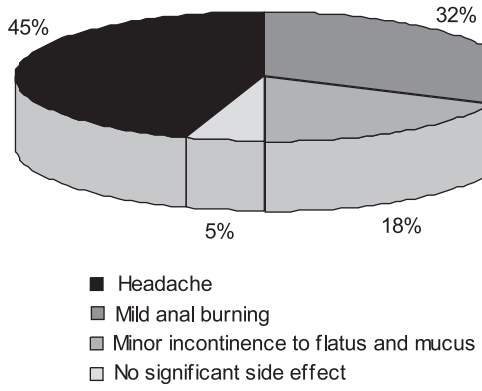

Fig.-2: *Side effects (n=122)*

Discussion:

Surgical sphincterotomy traditionally is the treatment for chronic anal fissure, lowering the resting anal pressure by as much as 26% to 50%. High rates of soiling of underclothes has been reported after this procedure[9]; though fissure heals within three weeks after the procedure.[1] Anal stretching is also attractive to some surgeons because of its extreme simplicity, but is associated with a number of unacceptable complications like bruising, infection, prolapse and incontinence. In recent years newer pharmacological agents have been developed to promote fissure healing by producing chemical sphincterotomy with the aim of avoiding long-term problem of incontinence. Chemical sphincterotomy has been tried using a variety of pharmacological agents including topical glyceryl trinitrate, calcium channel blockers such as nifidipine or diltiazem and botulinum toxins with variable responses. These agents were found to be effective in healing chronic fissure in a significant number of patients with minimal side effects. In several other studies, others are concerned about their use in particular the occurrence of side effects limit their use and unfortunately they are not always effective at healing fissure.[10] Nitric oxide donor GTN can produce reversible chemical sphincterotomy and has been reported to heal fissure by inducing sphincter relaxation and improving anodermal blood flow.[7,11] Reduction in anal pressure in chronic anal fissure has been shown to increase anodermal blood flow with resultant pain relief and early fissure healing.[6,7,8] In our study symptomatic relief occurred in 13.93% of patients at the end of 2 weeks topical application of 0.2% GTN without complete healing of fissure. Complete healing of fissure was noted after 4 weeks treatment and about one third of the patients had pain relief and healed fissure at 4 weeks treatment. Symptomatic relief occurred earlier than fissure healing. After 8 weeks of complete treatment about two third of the patients in the present series had successful chemical sphincterotomy. Rest of the patients did not experience significant benefit and were advised for surgical sphincterotomy. Though headache was an alarming side effect in a good number of patients (Figure 2), this did not make our patients to discontinue the treatment because of prior counselling. Mild anal burning and itching with

mucus discharge in some of the patients were acceptable so far they got relief from the annoying symptoms.

Conclusion:

Though surgical sphincterotomy is the traditional and most effective treatment for chronic anal fissure with healing of fissure in 3 weeks, we would like to suggest local application of 0.2% glyceryl trinitrate for the treatment of this surgical condition initially to ensure a reversible chemical sphincterotomy thus avoiding the long term morbidity of incontinence in surgical sphincterotomy.

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