

1.0 INTRODUCTION

Fissure in ano is a well recognized health problem not only in Zambia but the world over. At UTH, many patients with this diagnosis are seen each year. These patients are largely managed by surgeons.

By definition a fissure in ano or ano fissure is a longitudinal tear of the lower anal canal. It is one of the painful anal conditions resulting in a lot of discomfort and embarrassment to the patient [1, 2,]. The pain is sharp, agonizing during defecation and may last for an hour or more. The patient is comfortable until the next defecation. A period of remission may occur, usually for days or weeks. Severe pain during defecation usually makes the patient avoid defecating and this result in constipation, doing so with a fresh tear more likely during next defecation.

The etiology varies from diarrhoea, constipation, tight anal sphincter, trauma as in anal intercourse and child birth. Contrary to traditional teaching a precipitating history of constipation is found in 20% of patients [2]. Many a time's etiology cannot be identified.

Cases of fissure in ano are classified into acute and chronic. In some cases patients present with acute on chronic fissure in anal.

In acute cases, the history is usually short lasting less than 6 weeks. There is inflammation of the anal mucosa, slight induration and there is always spasms of the internal anal sphincter [2].

On the other hand, chronic cases presents with a long history lasting more than 6 weeks [1,2], there is an associated edematous skin tag known as sentinel pile, there is inflammation and marked induration of the margin and the base, spasm of internal anal sphincter may be there too. In chronic fissure differential diagnosis of other conditions particularly carcinoma should be considered. Acute on chronic anal fissures are very common.

Diagnosis is by way of digital and protoscopic examination, though painful and needs patient cooperation. Treatment is either conservative or surgical.

Conservative management includes topical GTN (glycerine trinitrate) cream and anaesthetic cream application, MDA (manual dilatation of anus), high fiber diet, sitz

baths and antibiotics. GTN increases NO (nitric oxide) which is a very potent muscle relaxant. It acts on vascular smooth muscle there by causing vasodilatation. This increases blood flow to the fissure hence facilitate healing [3,4,5,6].

MDA is a day care procedure, the patient goes home the same day. It is however associated with minor fecal incontinence in some patients lasting a week to 10 days hence the patient should be fore warned.

Surgical treatment is mainly by lateral sphincterotomy [1].

At The University Teaching Hospital (UTH), this condition is mainly treated by MDA in combination with sitz baths and high fiber diet. Topical GTN cream has an excellent effect to heal the fissure. Though it is an approved drug by the Pharmaceutical Regulation of Zambia (PRA), it is not on the market in Zambia [3]. Local anesthetics have been used to relieve pain but seem to be of little help [3].

The recommended concentration of GTN cream is 0.2 – 0.3%. Since it is not readily available locally, it can be made by crushing 210 tablets of glycerine trinitrate, 500micg each, which is then added to 20gm of KY jelly in a plastic container with a lid and left over night to dissolve in this water base jelly and in the morning stir the jelly. This makes 0.25% GTN .This has been used on some patients with excellent results [3].

The patient is instructed to take sitz baths for 10 minutes then apply this jelly with a gloved finger as far in the anus as possible at the same time massaging gently. This can be repeated 2- 3 times per day. This breaks the vicious cycle of spasmodic pain and difficult in passing stool thus encouraging the fissure to heal. The only disadvantage with GTN cream is that it causes headache in some patients [5]. If headache cannot be relieved by a pain killer, treatment should be discontinued.

Fissure in ano is a troublesome and a very painful condition that affects a great majority of the population world over. Its prevalence is difficult to estimate [7]. It occurs equally in both sexes and with no racial pre direction. It affects children equally as adults. However it is common in people who eat a lot of purified foods and less of fibrous foods.

The nature and the anatomy of fissure in ano are quite clear. Much is known about the various predisposing and contributing factors that lead to initiation and progression of the disease. The preferred method of treating the condition is the one that results in optimal clinical results and is least painful and causes little inconvenience to the patient. However, various methods of management have been debated widely [6]. The crack is usually in the posterior midline. Occasionally it may be anterior or on the lateral aspect [8]. About 90% occur in the posterior midline while about 10% occur in the anterior midline. Sex distribution is almost equal [2].

Anal fissure is the most common cause of severe anal pain. It is equally one of the most common reasons of bleeding per anus in infants and young children. The pain of anal ulcer is intolerable and is always disproportionate to the severity of the physical lesion. It may be so severe that patients may avoid defecation for days together. This leads to hardening of the stools, which further tear the anoderm during defecation, setting a vicious cycle [6]. Recent studies have highlighted the role of increased internal anal sphincter pressure and decreased anodermal blood flow in the pathogenesis of chronic anal fissures. The internal anal sphincter hypertonia seen in patients with an anal fissure has long been thought to be a secondary phenomenon, occurring after local trauma to the mucosa by passage of hard faeces. In this scenario, subsequent sphincter spasm then leads to further constipation and so a vicious cycle is created. Traditional treatment (anal dilatation and internal sphincterotomy) aims to break this cycle by disrupting the internal anal sphincter. Recent research [2] has shown the blood flow to the posterior midline of the anus is potentially deficient, being supplied by end arteries (mean arteriolar blood pressure 85 mmHg), which passes through the internal anal sphincter before reaching the posterior commissure. As the maximum resting anal pressure (MRAP) is usually greater than 90 mmHg in patients with fissures, such hypertonia will compress these end arteries and cause ischemia of the posterior commissure. Such a reduction in the posterior anodermal blood flow has been confirmed using laser Doppler flowmetry. Further evidence [9] that the hypertonia is not secondary to pain arising from the demonstration that it is not relieved by the use of topical anaesthetics. This evidence supports the hypothesis [10] that anal fissures are caused by internal anal sphincter hypertonia producing ischemia of the posterior commissure of the anus. This explains the presence of sphincter spasm. Spasms in the anal sphincter and ischemia due to insufficient blood supply to the area may be the helping factor in the development of fissure in ano and also

in preventing healing process [9, 11]. Anal fissures are also associated with diverticulitis, foreign body reaction, Actinomycosis, Chlamydia, Lymphogranuloma venereum, syphilis, tuberculosis, radiation exposure and HIV [2]. The fissures can be classified into acute or superficial and chronic.

1.1.0 ACUTE FISSURE IN ANO.

Predisposing Factors: It has been proved that constipation is the primary and sole cause of initiation of a fissure [2, 12]. Passage of hard stool, irregularity of diet, consumption of spicy and pungent food, faulty bowel habits, and lack of local hygiene can contribute to initiation of the pathology. In females, the ailment is usually triggered during pregnancy and following child birth as a superficial split in the anoderm that may heal by itself or may progress to a chronic fissure.

Pathophysiology: The anoderm is more adherent to the underlying tissue in the posterior midline. The sphincter fibers form Y-shaped decussation [2] in the posterior midline that is anchored to the mucosa. Blood supply to the anoderm at the posterior midline is significantly lower. The reduced blood supply to the lesion is indicated by the absence of granulation tissue at the base of the fissure and a very slow growth of the anoderm even when the traditional conservative treatment eases the trauma due to hard faeces.

A well-developed idiopathic anal fissure rests directly over the internal sphincter and the circular fibers of this sphincter are visible on the floor of the fissure on naked eye inspection. The internal sphincter undergoes a perpetual state of spasm due to irritation and hypertrophies.

Most anal fissures heal on their own and do not require treatment provided the patient observes a high standard of hygiene [13]. However for those that fail to heal on their own, the principle of management is to break the vicious cycle, thus allowing the fissure to heal by reducing the internal anal sphincter spasm [14].

Treatment of acute fissures: It has long been recognized that acute fissures can be cured conservatively [2,14]. Presence of anal tags and polyps is a contraindication to conservative therapy [14]. The following methods are usually advocated for simple

fissures.

- (i). Warm water sitz bath with or without adding boric powder, povidone iodine solution, or potassium permanganate in the water. This treatment soothes the pain and relaxes the spasm of the internal sphincter for some time.

Adequate analgesia is necessary to break the vicious cycle of pain thus avoidance of defecation for prolonged periods leading to hard stools resulting in further tearing of the anoderm and thereby inviting increased pain [2]. A suitable dose of analgesic consumed half an hour before going for defecation gives a good amount of post defecation pain relief.

- (ii). Stool softening is essential as soft and formed stools negotiate the rectum and anal canal in non-traumatic physiologic maneuver. Plenty of oral fluids also help in keeping the stools soft.
- (iii). High-fiber-diet and bulk-forming agents such as Isaphgula, green leafy vegetables and fibrous fruits go a long way in increasing the bulk of stool leading to a smooth and swift act of defecation [2]
- (iv). Reassurance and encouragement for not resisting the urge for defecation help prevent hard stools. Later the patient could be encouraged to acquire and maintain a regular bowel habit of once or twice a day. Application of local anesthetic cream or gel may help avoid the torture experienced in passage of stools in the patients with acute fissures. Ointments containing opiates, xylocain, amethocain, and cinchocain to relieve pain, belladonna to alleviate sphincter spasm and silver nitrate to promote healing have been in vogue since long. These mixtures are introduced on the finger or a short rectal bogie to ensure a through application over the desired part of the fissure. The modern practice is to insert the ointment over an anal dilator, which in addition helps relieve sphincter spasm. The possible complication of this treatment includes pruritus due to allergy with the anesthetic agents and loss of anal dilator in the rectum. Various ways of management are available which includes surgical and non surgical methods.

1.2.0 Local application of vasodilators: Nitric oxide is an important neurotransmitter mediating internal anal sphincter relaxation. It has been proved that chronic anal fissure is ischemic in origin due to poor blood supply and spasm of internal anal sphincter.

Nitric oxide (NO) donors such as glycerine trinitrate [GTN] or isosorbide dinitrate are known to cause a chemical sphincterotomy leading to healing of fissure [16].

A 0.2% GTN ointment applied twice to the anoderm for 6 weeks results in a complete healing in 98% of patients. A few patients do experience mild headache during therapy [17,18].

In a study to determine the usefulness of GTN conducted at King Khalid University Hospital Riyadh, Saudi Arabia [19], involving 121 participants with acute and chronic anal fissure and were treated with 0.2% GTN, the cure rate was 94.7%. Similar findings were recorded [11, 20, 21]. Adverse effects were noted in 4.3% of participants. This study concluded that GTN ointment produces adequate symptomatic control and healing of ano fissure and can be considered as one of the recommended treatment options.

In another study, Topical diltiazem ointment was used as an agent for chemical sphincterotomy for chronic anal fissure. The Study claims to offer significant healing rate and reduced incidences of side effects [1].

However, during the course of therapy, strict dietary restrictions [1] to smoothen the stool are necessary. Headache during therapy is a major concern with the incidence as high as 20 – 100%. Though the application of GTN has a high healing rate; it also has a high recurrence rate if the primary cause is not addressed.

A prospective randomized study [22], double blind placebo controlled trial in which 80 participants with chronic fissure in ano were recruited, healing rate was 68% at 6 weeks. A potential problem using GTN was poor compliance. 58% developed a headache at some point during the study while no cases of incontinence were reported.

In another prospective but uncontrolled study [23] conducted at polyclinic in Bahrain whose objective was to determine the efficacy of GTN ointment, 44 participants were treated with this preparation during the period June 2002 to August 2005. It was reported

that 73.5% had complete pain relief and 94% had normal anal tone. It was concluded that use of GTN ointment induces rapid healing of chronic fissure in ano with 82.4% healing rate. It was further noted that successful treatment comes at an expense of high incidence of headache.

In a similar five year prospective trial at PMC Faisalabad in 2001 patients were treated with 0.2% GTN and the cure rate was reported at 64.3%. All patients reported headaches which was mild in 71.4% and moderate in 28.6%. It was concluded that GTN preparation is safe and effective modality that can be considered as first line of treatment for fissure in ano especially in unfit patients or those who wish to avoid surgery.

1.3.0 Direct current probe treatment: This method is tried in patients of chronic anal fissures with associated internal hemorrhoids.

A study claims that when the DC (direct current) probe was applied to the internal hemorrhoids, the patients were relieved of anal pain and healing occurred in 90% of patients [2].

However, this mode of treatment requires special equipment and the procedure takes a very long time [about 10minutes for each hemorrhoid]. Moreover, the mechanism of action on the part of fissure is not understood.

1.4.0 Endoscopic anal dilatation: In this procedure, anal dilatation is performed with a two-valve anoscope under local anesthesia as an office procedure.

In the study, 93% patients were found symptom free one month after the procedure, and only a few had a recurrence [24].

This procedure is said to be free of discharge or incontinence either transient or permanent. In another series, a Parks' retractor or a recto sigmoid balloon has been used for sphincter dilatation. Out of 495 patients treated by this procedure, it was reported that in as many as 87–88% of the patients, the fissures healed within 3 months [25]. Literature is scanty in support of this technique. It will be improper to comment on the efficacy of this procedure.

1.5.0 Chemical cauterization: This is done by injecting silver nitrate or phenol-in-glycerin in the fissure. This procedure may be repeated a couple of times until healing occur. Usually it takes about 4 to 8 weeks for complete healing of the fissure. Accidental injection in the surrounding tissue leads to general poisoning, haematoma and infection. Surgeons refrain from regularly resorting to this method.

Operative Techniques:

1.6.0 Stretching of anal sphincter [Lord's anal dilatation]: Anal dilation was described by Recamier in 1838. This was one of the most favored and accepted methods of treating the anal fissures. The primary cause of attraction for this procedure is its simplicity [2, 6]. Since almost no instruments are needed for this procedure, it could be performed at the primary health centers or inadequately equipped hospitals situated at small centers.

Anal dilatation helps in healing of the fissure by reducing the anal canal pressure. If performed with due care by avoiding excessive manipulation, it does not cause any damage to the external anal sphincter. In experienced hands, incontinence of stools or flatus is seldom seen [2, 24].

However, recent studies have shown that anal dilation has a higher risk of fissure persistence and higher risk of incontinence [23, 24, 25]. In a study conducted to determine the best technique for anal fissure surgery [23], various surgical procedures were compared and the findings were that anal stretch (dilatation) had a higher risk of fissure recurrence than internal sphincterotomy and also had a significantly higher risk of minor incontinence than sphincterotomy. It concluded that anal stretch should probably be abandoned in the treatment of anal fissure. Although the procedure in itself is curative, in cases with associated pathologies, it has to be supplemented with an additional procedure, In a similar study conducted in Glasgow in the UK ,46 patients with fissure in ano under went anal dilatation .It was found that anal dilatation failed to treat 26(56%) patients [26].

1.7.0 Excision of the anal fissure [fissurectomy]: A triangular part of the anoderm is excised along with the fissure itself. This procedure is usually preceded by anal stretch. Howsoever, no matter how good and reliable this operation is, it leaves behind a large

and rather uncomfortable external wound, which takes a long time to heal.

1.8.0 Fissurectomy with immediate skin grafting: To expedite healing and shorten the convalescence, application of a split thickness graft to the wound is advocated by a section of the proctologists. The procedure is time consuming, rather a finicky one. It needs a hospital stay of about a week to keep patients bowel held up to avoid possible detachment of the graft. For these reasons, the procedure could not get enough acclamation and acceptance.

1.9.0 Division of internal anal sphincter: Division of internal sphincter fibers to relieve the sphincter spasm is presently considered the preferred therapy for chronic, recurrent and non-healing fissures [2, 27]. Two techniques have been described.

- A. Open posterior internal sphincterotomy. Posterior sphincterotomy is done by dividing the sphincter fibers through the fissure wound. The wound is slow to heal and has a tendency to lead to a posterior midline keyhole defect that may cause a persistent seepage or incontinence.

- B. Lateral subcutaneous internal sphincterotomy. It is one of the most favored procedures. The reasons for this are the simplicity of the procedure, minimal anesthesia requirements, and results are good. The lists of complications that can arise due to the procedure are formidable; but in careful and experienced hands these could be effectively handled [2]. The most common complications encountered are bleeding needing hospitalization, abscess and fistula formation, incontinence to flatus and feces, and recurrence.

Both the above procedures can be done either under a local or a general anesthesia depending upon personal preference of the surgeon based on his experience and the attitude of the patient.

1.9.1 Combined outpatient surgical and cyrotherapeutical treatment: A lateral anal sphincterotomy, which is done under local anesthesia, is followed by fissure curettage with N protosside cryosound. This is claimed to be quicker and more effective procedure. The additional maneuver is not found to be of any specific advantage.

1.9.2 Carbon dioxide laser surgery: It involves local laser vaporization of the fissure. The internal sphincter can be incised using this laser. In long-standing fissures, some degree of anal stenosis is present. It can be used to give relieving incisions in the three quadrants other than the fissure before the fissure is attended to. The high cost of the laser unit seems to be the major deterrent in its wider acceptance [2].

1.9.3 Lateral subcutaneous internal sphincterotomy and radio frequency surgery: In an attempt to improve on the available options, a fusion of method of sphincterotomy with radiofrequency is described. The procedure has been claimed to be effective in cases where the fissure is associated with pathologies like sentinel tags, hypertrophied anal papillae, fibrous polyps, post fissure fistula or internal hemorrhoids which can be tackled simultaneously while the fissure is being treated [2].

The radio frequency surgical unit uses *Ellman Dual Frequency 4MHz*. International [Hewlett, NY]; unit incorporates threefold function of cutting, cutting and coagulation or just pure coagulation. It is claimed that the fibrosed edges of a chronic fissure can be refashioned with the help of the radio frequency surgery. The entire procedure is quick and is virtually bloodless. This new treatment modality awaits further evaluation.

2.0 STUDY JUSTIFICATION

Fissure in ano is a common surgical condition in Zambia. At UTH patients commonly presents in acute attack. Treatment for this acute condition is mainly by MDA. The table 1 below shows the annual MDA that were done in the past 6 years, 2005 to 2010 in phase 5 theatre at UTH.

Table1: Annual number of MDAs done at UTH from 2005 to 2010

YEAR	NUMBER OF MDA
2010	91
2009	78
2008	60
2007	73
2006	82
2005	84

. There is no readily formulated GTN cream on the market, but it can be made easily using GTN tablet with relatively good results [3].

Fissure in ano is such a huge burden to surgical practice. At UTH, 78 manual dilatation of anus were performed in 2009 alone, 91 cases in 2010. Generally cases are on an increase. This treatment is an expensive way of treating this condition. Anal fissure in cases will continue to present at UTH. Further cases mean the burden and financial strain continues on this poor resource third world hospital. Therefore there is need to find a potent cost efficient solution to this problem. GTN cream has shown to be a practical solution to this problem. GTN (Glycerine Trinitrate) is more potent in the conservative management of fissure in as shown elsewhere [11, 16,17, 18, ,19]. It is not being used in Zambia because it is not commercially available on the market. However it can be made easily even at home by crushing GTN tablets which are available and dissolving the powder in KY jelly. GTN is an effective, safe and inexpensive. This study basically wishes to compare the effectiveness of this locally made GTN preparation in treating acute anal fissure to the current practice by MDA.

The following constitute a strong case why this study needs to be conducted:

- (i). Findings of this study could help in the designing of a protocol for the management of acute fissures in ano at UTH and periphery health institutions which is not available currently.
- (ii). UTH and periphery health facilities would cut costs towards labour, oxygen,

anesthesia, and consumables.

- (iii). Patients would avoid the risks associated with anesthetic agents.
- (iv). Risk to medical transmission of HIV would be reduced. The HIV (human immune virus) prevalence rate in Zambia is quiet high currently at 14.3% [28].
- (v). The study might be used as baseline for future studies on this pathology.

3.0 RESEARCH QUESTION

Is locally made GTN cream potent and cost effective in treatment of acute fissure in ano than treatment by MDA?

4.0 OBJECTIVES

Specific objectives;

- (i). To study the out come of treatment for fissure in ano with locally made GTN cream and treatment with MDA treatment methods.

Secondary objectives;

- (i). To determine the demographic characteristics including HIV status of patients with fissure in ano presenting at UTH.
- (ii). To compare the treatment outcomes for the two methods, the MDA and GTN.
- (iii). To assess the complications associated with each of these methods.
- (iv). To determine the cost of each of these treatment methods

5.0 RESEARCH METHODOLOGY

Study type – A randomized controlled trial.

Site – The University Teaching Hospital (UTH), Lusaka.

Study duration and setting – The study was conducted from 16th August, 2011 to 13th April, 2012. A fissure in anal clinic was set up at clinic 4 which operated every Friday from 14.00 hours to 16.00 hours. Participants were referred to the clinic for screening and recruitment by clerks as well as by Doctors in the department of surgery.

Case definition – Males and females 18 years and above who presents with acute anal pain and with clinically diagnosed fissure in ano were considered for recruitment provided they met the inclusion criteria.

Inclusion criteria

- Participants 18 years old and above presenting at UTH.
- Clinical diagnosis of fissure in ano with symptoms of up to 6 weeks duration.
- Participants who consent for inclusion

Exclusion criteria

Participants with the following characteristics were not considered for inclusion in the study.

- Those not fit for surgery
- Those with pre existing headache

Data collection: A total of 73 patients (see figure 1) were screened for participation but only 69 met the criteria for inclusion. Of these, 68 accepted to take part in the study while 1 declined. This figure include the 5% (4 participants) expected loss to follow up.

The sample size was calculated using the Open Epi version 2 software as illustrated in the table below. Of these, thirty four (34) were allocated to the intervention group (GTN cream) while the other thirty four (34) allocated to the control group (MDA).

(a). Sample size determination

Table 2: Method of sample calculation using Open Epi, Version 2, open source calculator—SSCohort

Sample Size for Cross-Sectional, Cohort, & Randomized Clinical Trial Studies		
Two-sided significance level (1-alpha):	95	
Power (1-beta, % chance of detecting):	80	
Ratio of sample size, Unexposed/Exposed:	1	
Percent of Unexposed with Outcome:	60	
Percent of Exposed with Outcome:	90	
Odds Ratio:	6	
Risk/Prevalence Ratio:	1.5	
Risk/Prevalence difference:	30	
Fleiss		
Sample Size - Exposed	32	
Sample Size-Non exposed	32	
Total sample size:	64	
References		

(b). Sample selection and allocation

Participants who met the inclusion criteria and had given an informed consent were randomized. Allocation to the two groups was done by block randomization. This was done by computerized random number generator using blocks of four. This generated 17 blocks in total for a sample size of 68 participants. For every four drawn, two were allocated in the glycerine trinitrate (GTN) group while the other two in the manual dilatation of anus group (MDA).

Numbers 1 to 68 were written on pieces of paper, then placed in opaque envelopes. Enrolment basically was done as the participants were recruited. Once recruited, a participant was asked to pick an envelope in the order as generated by the computer. The envelope was then opened to reveal the number contained. Odd numbers were for MDA while even numbers for GTN allocation.

(c). INTERVENTION AND CONTROL

(i). Management of Intervention (GTN) Group.

GTN cream preparation – Topical 0.25% GTN Was prepared by crushing 210 tablets of GTN, 500mcg each then adding it to 20gm KY jell in a plastic container with a lid and left over night to dissolve in this water based jelly. The preparation was then stirred the following morning. Preparation of the GTN cream was done by the UTH pharmacy. The GTN cream was to be stored in room temperature and used within 1 months of preparation.

Initial Management

- Participant in this group were treated with GTN cream.
- Application of 0.25% GTN cream was demonstrated to each participant.
- It had to be applied on a gloved finger as deep in the anal canal as possible.
- The participant was then requested to recite the application procedure to ensure they understand how to administer the GTN cream correctly.
- In addition they were advised to take a sitz bath for 10 minutes prior to application of the cream. GTN cream had to be applied twice daily.
- When sure that the participant had understood the process of application, they were then supplied with gloves and GTN enough to last for 2 weeks.
- Observation of high standard of hygiene and a intake of high fibre diet was emphasized to all participants.

Participants were then reviewed at 2, 4 and 6 weeks in clinic 4. Findings during each

review were entered in the questionnaire

(ii). Management of Control (MDA) group.

Initial management

- Participants in this group were allocated a day and time for phase 5 theatre at UTH. All usual preparation which also included consent for theatre were done.
- The anus was dilated up to 4 fingers for a duration of 1 minute under GA (general anaesthesia) by the researcher.
- 1ml 0.5% lignocaine was then injected at the base of the fissure to relieve pain expected soon after general anaesthesia wears off post MDA.
- After MDA, participants were allowed home the same day on 1g paracetamol to be taken 6 hourly for three days.
- At time of discharge, participants were advised to observe a high standard of hygiene, take sitz baths twice a day for 10 days and to include food with high fibre content in their diet.

They were then reviewed at clinic 4 at 2, 4 and 6 weeks post operatively. During each review, findings were entered in the questionnaire.

(d). Follow up of participants

1. During each review, the following were enquired from participants for both groups.
 - (a). If there was an improvement or not in their condition.
 - (b). The kind of diet they have been taking.
 - (c). If they have been having sitz baths as prescribed.
 - (d). If they were still having anal pain. Also if pain was felt;
 - (i). At time of defecation.
 - (ii). Is associated with constipation.
 - (iii). Is there at all times.
 - (e). If there has been anal pain, its severity was determined.
 - (f). If they had experienced any episodes of fecal or flatus incontinence.
 - (g). If they had been experiencing headache, if so severity determined.

2. The participants were then examined with emphasis on the following.

- (a). Determination of absence of fissure tenderness .
- (b). State of anal sphincter – If normal tone, hypotonic or hypertonic.
- (c). If tenderness was present, its severity was determined

Examination findings were also entered in the questionnaire at 2, 4 and 6 weeks reviews.

Pain;

Pain in this context was graded as follows;

0 – Pain free

Mild pain – pain nagging, annoying but does not interfere with daily living
Activities

1 – Pain is very mild, barely noticeable. Most often you do not think about it.

2 – Minor pain. Annoying and may have occasional strong twinges

3 – Pain is noticeable and distracting, however one can get used to it and
Adapt

Moderate pain – Interferes significantly with daily living activities

4 – Moderate pain. If one is deeply involved in an activity, it can be ignored
for a period of time, but is still distracting

5 – Moderately strong pain. It cannot be ignored for more than a few
minutes, but with effort one is still able to work or participate in some
social activities

6 – Moderately strong pain that interferes with daily activities. Difficult
Concentrating

Severe pain – Disabling, unable to perform daily living activities

7 – Severe pain that dominates your senses and significantly limits your ability
to perform normal daily activities or maintain social relationships.

Interferes with sleep

8 – Intense pain. Physical activity is severely limited. Conversing requires great
Effort

9 – Excruciating pain. Unable to converse. Crying out and/ or moaning
uncontrollably

10 – Unspeakable pain. Unable to converse. Bed ridden and possibly delirious.

Very few people will experience such kind of pain

Tenderness – Was graded as follows.

0 – No tenderness

Mild tenderness

I – Complaint of pain on palpation

II - Complaint of pain - winces / grimace

Moderate tenderness

III – Complaint of pain - winces / grimace and withdraws

Severe tenderness

IV – Withdraws (jumps), or will not allow palpation

Fissure healing – Total resolution of pain.

(e). Data analysis

(i). Dependent variables

- Age, sex, HIV status, headache, fecal incontinence, flatus incontinence, baseline anal fissure pain and tenderness, treatment compliance.

(ii). Independable variables

(a). Primary outcome

- Anal fissure healing by end of 6 weeks

(b). Secondary outcomes

- Failure for the fissure to heal
- Fecal incontinence at 2, 4 and 6 weeks
- Flatus incontinence at 2, 4 and 6 weeks
- Headache at 2, 4 and 6 weeks
- HIV status

6.0 DATA ANALYSIS

Data collection tool: Data was collected using a self administered semi-structured questionnaire and then entered into the data master sheet

Data entry and processing: Data was entered into Epi info computer software for processing .

Data cleaning: Editing of data was done using range checks and consistent

Measurement of association: Relative risk (RR) was used to measure associations at 95% confidence level.

Comparison of baseline data: Baseline information was compared between the two groups using the chi-square test for quantitative variables while the t-test was used to compare means of continuous variables. Significance was assumed when p-value was $<$ or $= 0.05$

7.0 RESULTS

7.1: Enrolment

Seventy three (73) participants were scrutinised for enrolment [Figure1 below] but only sixty nine (69) satisfied the entry requirements. The rest were unable to satisfy the requirements because of various reasons which included previously having been treated for the same condition, presence of associated anal lesions other than fissure in ano, poor general health and presence of headache.

Of those who met the inclusion criteria, one (1) declined participation without giving a clear reason despite being availed full information concerning the study. Finally sixty eight (68) participants consented for participation and all were followed up to the end point of the study.

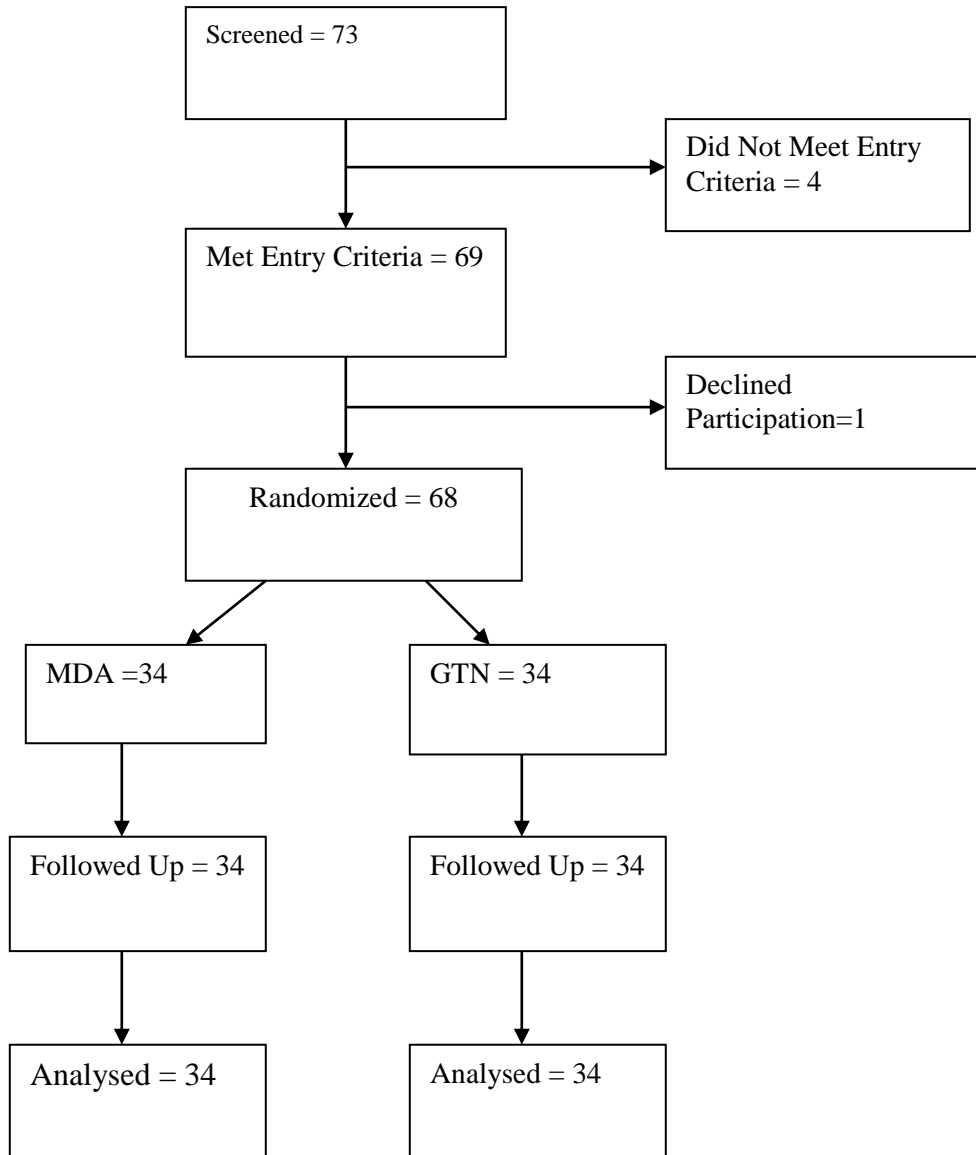


Figure 1: Flow diagram of the progress through the phases of parallel randomized trial MDA vs GTN for acute fissure in ano.

7.2 : baseline characteristics of the participants

Baseline characteristics considered to be of relevance to this study included sex distribution, age, HIV status, presence or absence of constipation and site of fissure.

Sex distribution was fifty percent (50%) for each. The mean age was 31.8 [see table 3]. The HIV prevalence was thirteen point two percent (13.2%) which compares well with the nation prevalence of fourteen point two percent (14.2%) as reported by the Zambia Health and Demographic Survey for 2007 [28].

Four participants (5.9%) declines to take the HIV test. Three (3) of them felt that they needed to consult their spouses before they could consider participation. Unfortunately consent was not given and consequently could not take part. The other one who happened to be a collage student said she could only take the test after completing of her studies. All the four (4) were however successfully treated by MDA.

Table 3: Baseline characteristics for 68 participants with acute fissure in ano

randomized to MDA vs GTN

VARIABLE	TOTAL(n=68)	MDA(n=34)	GTN(n=34)	p-value
SEX				
Male	36(52.9)	17(50.0)	19(55.9)	0.62
Female	32(47.1)	17(50.0)	15(44.1)	
AGE (years)	31.8(9.2)	32.1(9.1)	31.5(9.5)	0.80
HIV STATUS				
Non reactive	55(80.9)	27(79.4)	28(82.40)	0.94
Reactive	9(13.2)	5(14.7)	4(11.8)	
Unknown	4(5.9)	2(5.9)	2(5.90)	
CONSTIPATION				0.50
Constipated	61(89.7)	30(88.2)	31(91.2)	
Not constipated	7(10.3)	4(11.8)	3(8.8)	
SITE OF FISSURE				
Posterior	49(72.1)	24(70.6)	25(73.5)	0.77
Posterior/lateral	8(11.8)	5(14.7)	5(14.7)	
Posterior/anterior	4(5.9)	2(5.9)	2(5.9)	
Anterior	4(5.9)	1(2.9)	3(8.8)	
Lateral	2(2.9)	1(2.9)	1(2.9)	
Anterior/lateral	1(1.5)	1(2.9)	1(2.9)	

*All variables are reported n (%), except age which is shown as mean (SD)

As regards position of fissure, the majority (89%) of the participants had fissure located in the posterior position [table 1]. This finding is in agreements with what is reported by literature [2,7]. Thirteen (13) participants had more than one (1) fissure in ano

7.3 : Cost of treatment per participant MDA vs GTN

Table 4: *Costs of treating a participant by MDA compared with locally made GTN cream*

TREATMENT	ITEM AND COST (KR)	TOTAL (KR)
MDA	Anaesthesia Labour Consumables	800
GTN cream	60 GTN tablet KY jelly (20ml tube) Labour: GTN cream preparation Consumables	192

**All values are in 2013 Zambian kwacha rebased (KR). Note that labour costs for the surgeon and nurses include screening, theatre and review costs.*

Table 4 above illustrates the cost of treating a participant with MDA and with GTN cream. Treatment by MDA for each participant required KR800 while with GTN cream required KR192. It is therefore very clear that treatment of fissure in ano with GTN cream is far much cheaper compared to treatment by MDA.

7.4: Responsency to treatment

The results as shown below [Table 5], the primary outcome at six (6) weeks shows that fissure in ano treatment with GTN gives a relative risk of 1.11 (0.91-1.33) meaning that it has the same outcome as compared to MDA. Prior to six (6) weeks, GTN does not show good responsency as is shown by the RR of 0.22 (0.05-0.95), 0.41 (0.22-0.75) at two (2) weeks and four (4) weeks respectively.

As regards improvement of fissure pain with treatment, quicker resolution of symptoms was observed in the MDA group at two (2) and four (4) weeks compared with the GTN group. However it was observed that improvement was the same at about six (6) weeks for both groups. All participants had reported improvement of symptoms at the end of six (6) weeks [Table 5].

Table 5: Outcome for 68 participants with acute fissure in ano after treatment with MDA and GTN cream.

#VARIABLE	MDA(n=34)	GTN(n=34)	RR (95% CL)
Fissure healing at			
2 weeks	9(26.5)	2(5.9)	0.22 (0.05-0.95)
4 weeks	22(64.7)	9(26.5)	0.41 (0.22-0.75)
6 weeks	28(82.4)	31(91.2)	1.11 (0.91-1.33)
Improvement of symptoms at			
2 weeks	33(97.1)	27(79.4)	0.8 (0.68-0.98)
4 weeks	33(97.1)	34(100.0)	-
6 weeks	34(100.0)	34(100.0)	-

Table 5 continued

VARIABLE	MDA(n=34)	GTN(n=34)	P value
Fissure pain at			
2 weeks			
None	8(23.5)	3(8.8)	P=0.02
Mild	21(61.8)	19(55.9)	
Moderate	3(8.8)	6(17.6)	
Severe	2(5.9)	6(17.6)	
4 weeks			
None	21(61.8)	9(26.5)	P=0.01
Mild	11(32.4)	21(61.8)	
Moderate	2(5.9)	4(11.8)	
Severe	0(00.0)	0(00.0)	
6 weeks			
None	28(82.4)	30(88.2)	p=0.08
Mild	6(17.6)	2(5.9)	
Moderate	0(00.0)	2(5.9)	
Severe	0(00.0)	0(00.0)	

Table 5 continued

VARIABLE	MDA (n=34)	GTN (n=34)	P value
Anal sphincter tone at			
2 weeks			
Hypertonia	16(47.1)	27(79.4)	P=0.43
Normotonia	18(52.9)	7(20.6)	
Hypotonia	0(00.0)	0(00.0)	
4 weeks			
Hypertonoa	6(17.6)	6(17.6)	P=0.40
Normotonia	28(82.4)	28(82.4)	
Hypotonia	0(00.0)	0(00.0)	
6 weeks			
Hypertonia	1(2.9)	0(00.0)	P=0.45
Normotonia	33(97.1)	34(100.0)	
Hypotonia	0(00.0)	0(00.0)	
Headache at			
2 weeks			
None	34(100.0)	29(85.3)	P=0.11
Mild	0(00.0)	5(14.7)	
Moderate	0(00.00)	0(00.0)	
Severe	0(00.0)	0(00.0)	
4 weeks			
None	34(100.0)	31(91.2)	P=0.05
Mild	0(00.0)	3(8.8)	
Moderate	0(00.0)	0(00.0)	
Severe	0(00.0)	0(00.0)	
6 weeks			
None	34(100.0)	34(100.0)	P=0.09
Mild	0(00.0)	0(00.0)	
Moderate	0(00.0)	0(00.)	
Severe	0(00.0)	0(00.0)	

All the baseline characteristics gave a P- value of < or = 0.5 meaning that there was no

significant difference in characteristics between the two cohorts. In other words, the characteristics of participants in the two groups were comparable.

In terms of outcome, there is significant difference for most of the variables since P-values are <0.5 at 0.98 at six (6) weeks.

Six participants under the GTN group experienced mild headache during the course of treatment which is attributed to glycerine trinitrate [Table 5]. Five (5) had headache in the first two weeks of treatment while one had headache during the third and fourth week. All the patients who had developed headache were successfully treated with paracetamol and were able to continue with fissure treatment.

7.5: Pain reduction rates (MDA vs GTN cream)

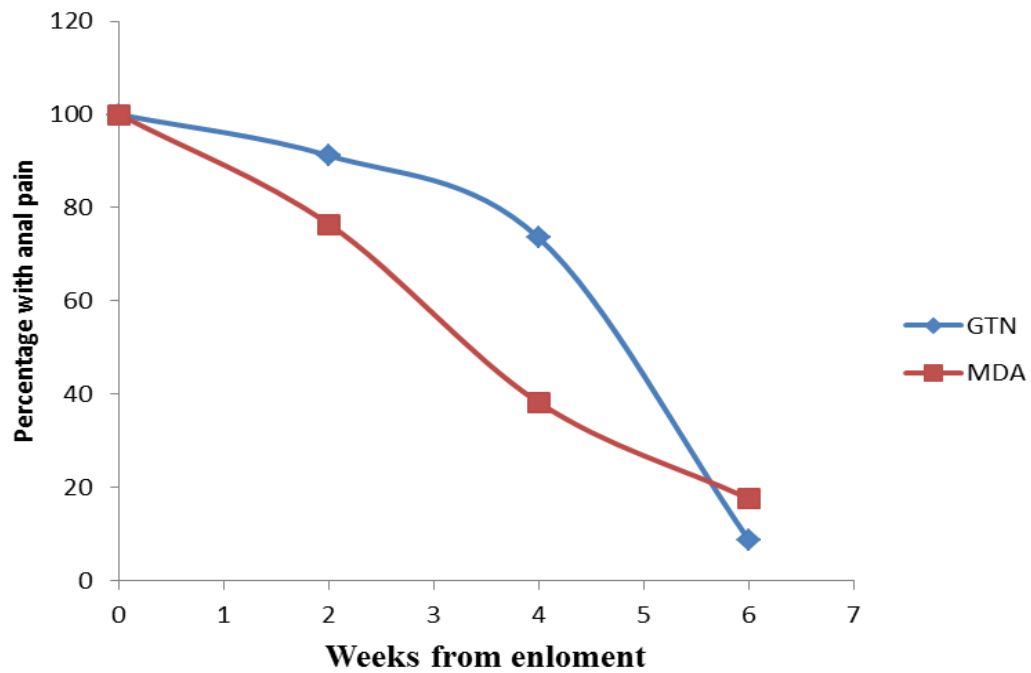


Figure 2: Rates of healing during treatment with MDA and GTN.

From Figure 2, it is evident that rate of fissure healing is faster for the MDA as compared to the GTN group during the first four (4) weeks of treatment. At day 40, the rate of healing is the same for the two groups and beyond that, healing is faster with GTN cream.

8.0 DISCUSSION

This study was conducted within the stipulated time and progressed to completion incident free.

The relative risk (RR) of 1.11 (0.91-1.33) basically mean that means that there is no significant difference in the outcome between these two methods. In other words, treatment outcome for the two methods is the same. Both methods are effective in treating acute fissure in ano.

The cure rate with locally made GTN cream was 91.2%. This agrees with UTH study by Prof G. Desai and Akhtaev which reported effectiveness with locally made GTN cream in the treatment of acute fissure in ano [3]. A much higher cure rate of 98% and 94% with commercial GTN cream has been reported [7] and [17] respectively.

Since the aim of treatment is to relieve pain as soon as possible, MDA should be maintained as standard treatment for acute fissure in ano since pain remission is faster with this method.

Despite the fact that it is cheaper to treat acute fissure in ano with locally made GTN cream [Table 2] as compared with MDA, it would be prudent to only consider GTN cream as a treatment modality for acute fissure in areas where theatre facility is not available or in a situation where the patient is unwilling to under go MDA.

It is clear that respondency to treatment with cheaper locally made GTN cream comes at an expense of delayed healing [Figure 2]. It could be argued that in our setting MDA is not guaranteed on the day acute fissure in ano is diagnosed in view of shortage of man power, limited operating time and long waiting operating lists stretching in months. Regarding treatment with GTN cream, treatment could be initiated immediately the diagnosis is made and consent is obtained.

Therefore initiation of treatment with locally made GTN cream would also be justified where MDA cannot be available immediately it is required though theatre facility is available.

Both methods work on the principle of increasing blood supply to the fissure. Increasing blood supply means more oxygen and nutrients delivery to the fissure which are prerequisite for healing. Earlier remission of fissure in ano with MDA can be explained by the fact that anal stretch relaxes the internal anal sphincter immediately the procedure is performed thereby allowing appreciable vasodilation hence increased blood supply to the fissure. Whereas for GTN cream, vasodilatation is gradual because of the hypertonicity of the internal anal sphincter. The cure rates with MDA being was 82.4% (28) which does not agree with Glasgow, UK study [26] which reported a failure rate of 56%. It also does not agree with [23] who reported higher failure rate and concluded that anal stretch should be abandoned in the treatment of fissure in ano.

Other studies [23, 24, 25] reported higher incidences of recurrence associated with MDA but this study did not look at recurrences after treatment. Perhaps another study could be carried out to assess recurrence after treatment.

In view of the higher cure rates reported by this study and the fact that pain relief is earlier with MDA, it is prudent to maintain MDA as a standard treatment for acute anal fissure. In other words, MDA should not be abandoned as has been suggested by other studies [23].

The majority (89%) of the participants were observed to have fissure posteriorly or at six o'clock position which is agreeable with findings in other studies [2,6,13]

Of those (9 participants) who did not get healed at the end of 6 (six) weeks, they all reported significant pain relief which had declined to bearable levels. The 3 participants (three) under the GTN cohort were pain free after repeat treatment. Of the 6 (six) under the MDA cohort, 2 (two) got healed after repeat MDA, 1(one) got healed after lateral sphinterotomy, 1 (one) is still being followed up while 2 (two) were lost to follow up.

As for the complications, only mild headache was observed in 6 (six) participants during the course of treatment of the GTN cohort. This agrees with findings as reported in other articles [17, 18, 22] associated with use of topical GTN cream. However severe headache was never reported. In a situation were it is observed, discontinuation of treatment is recommended. Those with pre existing headache should not be allowed to participate

especially for the GTN cohort as they are likely to develop severe persistent headache. Severe headache would interfere with treatment compliance and therefore affect treatment outcome as well as overall outcome of the study. Cases of headache reported were generally mild and participants were successfully treated with paracetamol. No new complications were observed.

Other complications such as fecal incontinence or flatus incontinence as reported by other studies [23, 24, 25] or articles were not observed. Incontinence has been reported when a probe is used for ano dilatation.

In order to aid healing and maintain the patient in remission, strict dietary restriction to smoothen stool is required. All the participants in this study reported adherent to high fibre diet. This must have contributed to high healing rates and anal fissure pain relief in all the participants.

9.0 CONCLUSION

1. Locally made topical 0.25% GTN cream is equally as effective in acute fissure in ano treatment as MDA
2. Effectiveness of locally made topical 0.25% GTN cream is at an expense of delayed responsency to treatment as compared to MDA
3. Therefore MDA should be maintained as a standard treatment for acute fissure in ano at UTH and periphery hospitals with theatre facility
4. Locally made topical 0.25% GTN is effective, cheap and safe, hence should be adopted for use in treating acute fissure in ano only in periphery hospitals where theatre facility is not available or when a patient with this condition is unwilling to be treated by MDA

10.0 RECOMMENDATIONS

The following are recommended

(A). MOH

1. MDA should be maintained as standard treatment for acute fissure in ano at UTH and periphery hospitals where theatre facility is available
2. Locally made GTN cream should only be used where a patient with acute ano fissure is not willing to under go MDA or in periphery hospitals without theatre facilities
3. To ensure commercial GTN cream is made available to UTH and periphery hospitals

(B). UNZASOM

1. A study should be carried out to compare the effectiveness of locally made GTN cream and commercial GTN cream
2. A study should be carried out to look at rates of recurrence after treatment with both MDA and locally made GTN cream
3. A study should be carried out to determine if GTN cream is effective in treatment of chronic fissure in ano

11.0 REFERENCES

1. Soln N, Weistein M. Anal dilatation for anal fissure. Seminar in colon and rectal surgery. 1997; (8): 17 – 23.
2. Igrid Legall. Anal fistula and fissure; Drugs, Disease and Procedures. Florida Hospital; Medscape. 2010;53(8):1110-5
3. Desai G. and Akhtaev A. Management of acute anal fissure - a personal view. Med J Zam 2008;35;1:34
4. Mohammad H.E, Samar, Chronic anal fissure, new approach to chemical sphincterotomy. JRMS, 2008;13(3);149 – 155
5. Orlay G. Anal fistula/fissure in ano. Colo rectal proctology and endoscopic clinic. 2005;48:108-13
6. Pravid J.G. Treatment of fissure in ano revisited; Africa Health Sciences. 2005; 4(1): pp58 – 62.
7. Elizabeth B and Renald B. Anal abscess and Fisttulas. 2012;16:14
8. Thomas J.P.S, Nicholls R.J and William C.B. Anal fissure in colorectal disease. London William Heinmann Medical Books Limited.1981; p 312
9. Prohn W.R, Bonner C. Is manometer essential for surgery of chronic ano fissure? Dis colon Rectum. 1995; 38:735 – 738
10. Collop B, Ryan P. Comperison of lateral subcutaneous Sphincterotomy with anal dilatation in the treatment of anal fissure. Med J Aust, 1979; (2):461 – 487.
11. Gough M.J. The conservative treatment of fissure in ano; Br J Surgery Society limited. 2005.vol70. Issue 3.pp175-6
12. Jensen SL. Diet and other risk factors for fissure in ano. Prospective case control study. Dis colon Rectum, oct1988; (10):770 – 773 [Pub Med]
13. Lippincott W and Wilkin. Anal fissure.Epub. Int J Sci.2009;6(2)77-84
14. Thomas C.B, Dehn. Ano fissure. Med lib online. 2006
15. Thomas J.P.S, Nicholls R.J and Williams C.B. Ano fissure in colorectal diseases. London Williams Heinmann Medical Books Limited.1981; p312
16. Bacher H, Mischinger H, J, Werkgartner G. Local nitroglycerine for treatment of anal fissure an alternative to lateral sphincterotomy. Dis colon Rectum. 1997;40:840 – 45
17. Ward D.L, Miller B.T, Cohen J, R. The use of glyceryl trinitrate in the treatment

- of acute and chronic anal fissure. Australian NZ Surgery. 2000;70:19 – 20
18. Cook T.A, Humphrey M.M, and Mc Mortensen. Oral nifedipine reduces resting anal pressure and heals chronic anal fissure. Br J Surg 1999; 8(10):1269 – 1274
 19. Knight J.S, Birks M, Farouk R.T. Tropical diltiazem ointment in the treatment of chronic ano fissure. Br J surg 2001 April 8(4):553 – 556 [Pub Med]
 20. Suhair Al-saad, Hamdi Al- shenawi, Mirrium Junaid and Deena Rashid: Use of glyceryl trinitrate ointment in the treatment of chronic fissure in ano. Bahrainm medical Bulletin, 2006; vol 28: No4.
 21. Machicado G.A, Cheng S, Jensen D.M. Resolution of chronic anal fissure treatment of contiguous internal haemorrhoids with direct current probe. Gastro intes Endosc. 1997; 45(2):157 – 162.
 22. Saad A.M, Omer A. Surgical treatment of chronic ano fissure. A prospective randomized study. East Africa Med J. 1992 Nov69(11); 613 – 615:107 – 108 [Pub Med]
 23. Farouk R, Gun J and Duthie G. Changing patterns of treatment for chronic anal fissure. Anna R Coll Surgery Eng, (1998); 80 pp194 – 196.
 24. Sharon Stein. Disease of colon and rectum. American Society of colon and rectum Surgeons. 2012,P01/08
 25. Nelson R. Operative procedures for fissure in ano. Condras data base syst. (2002); (1) CD002199 [Pub Med]
 26. McDonald A, Smith A, McNeill I. A. D and Finday I.G. Manual Dilatation of Anus. British Journal of surgery: volume79 issue12, pp1381 – 1382:2005
 27. Raymoony A.E. Surgical treatment of ano fissure under local anaesthesia. Sandi Med J.2001; 22(2):114 – 116. [Pub Med]
 28. Zambia Demographic and Health Survey (DHS-2007), pp 69-78

**12.0 APPENDIX I: QUESTIONNAIRE
RANDOMISED CONTROLLED TRIAL COMPARING LOCALLY MADE
GLYCERINE TRINITRATE TREATMENT TO MANUAL ANAL
DILATATIONFISSURE IN ANO CONDITION AT UTH.**

ENROLMENT DATE :..... SERIAL NUMBER :.....

Tick in appropriate box

1. Sex : M F
2. Age ;..... years
3. Where do you stay ?
4. What is your HIV status; Reactive None reactive
5. If reactive, WHO stage; I II III IV
6. For how long is the anal pain of pain? week (s).
7. Grading of anal pain; Mild Moderate Severe
8. Is anal pain association with the following?
 - (i). Constipation; Yes No
 - (ii). Defecation; Yes No
9. Fecal incontinence; Yes No
10. Are you having flatus incontinence? Yes No
11. Are you having headache? Yes No
12. Number of fissure(s)
13. Site of anal fissure; Posterior Anterior Lateral
14. Anal tenderness; Yes No
15. Grade of anal tenderness; Mild Moderate Severe
16. Anal sphincter tone; Hypotonia Normal tone Hypertonia

DATE POST INITIATION OF TREATMENT

Tick in appropriate box

1. Is there an improvement in condition of anal fissure? Yes No
2. Have you been compliant with regards to the following?
- (i). High fibre diet; Yes No
- (ii). Sitz bath; Yes No
- (ii). GTN cream compliance; Yes No
3. Is there anal pain? None Mild Moderate severe
4. Is there the following in addition to the anal pain?
- (i). Constipation; Yes No
- (ii). Defecation; Yes No
- (iii). Anal pain is constant; Yes No
5. Are you having headache? None Mild Moderate severe
6. Is there fecal incontinence? Yes No
7. Is there flatus incontinence? Yes No
8. State any other complications experienced below;
- (i).....
- (ii).....
9. Anal tenderness; None Mild Moderate Severe
10. Anal sphincter tone; Hypotonia Normal tone Hypertonia
11. Anal fissure healed; Yes No

13.0 APPENDIX II: PARTICIPANT INFORMATION SHEET

TITLE OF STUDY: RANDOMISED CONTROLLED TRIAL COMPARING LOCALLY MADE GLYCERINE TRINITRATE TREATMENT TO MANUAL ANAL DILATATION IN FISSURE IN ANO CONDITION AT UTH

INTRODUCTION; My name is Enock W. Soko, a post graduate student in general surgery at the University of Zambia (UNZA). The study is being carried out to find best treatment options for this condition in the country. The study will take place for 8 weeks. After enrolment, the participants are going to be reviewed at 2, 4 and 6 weeks. Each participant can only be subjected to one of the two forms of treatment being compared. Allocation shall be done randomly. For this study to yield meaningful results, it is required that all participants adhere to treatment. I am grateful to you for volunteering to take part in this study.

VOLUNTARINESS AND COMPENSATION: Participation in this study shall be purely on voluntary basis. In an event that treatment fails or a participant suffers a serious side effect, no compensation shall be given.

PURPOSE: To assess which of the two methods being considered has a better and cost effective outcome for treatment of fissure in ano.

BENEFITS; Both methods might treat your fissure in ano as they are already established treatment methods, hence you and indeed other people stand to benefit. The hospital may also benefit.

Note that there will be no monetary or material benefits for taking part in this study.

RISKS; The risks may include failure for the fissure to heal and occurrence of unknown side effects. These forms of treatment may also cause usual side effects which include flatus incontinence, fecal incontinence, and headache. However should they arise, they will be treated with standard treatment available.

RISK MITIGATION: In an event that prescribed treatment fails, other established methods which include surgical methods may be considered for any particular participant. The goal is to ensure all participants get treated of this condition. In order to mitigate side effects or adverse effects, participants shall be subjected to standard treatment. Participants shall be encouraged to report side effects or any strange occurrence. Side effects shall be treated with available standard treatment. However as for any strange occurrence which is fatal, treatment shall be discontinued immediately.

REFUSAL TO TAKE PART; This shall not in any way disadvantage you from seeking medical attention at this institution. You are also free to cease to take part in this study at any time even for no reason at all.

14.0 APPENDIX III: CHIZIWITSO CHAOTENGAPO MBALI PA

PHUNZILO

MUTU WA PHUNZILO: Mosayembekezela Kulinganiza kuyesa Glycerine Trinitrate ndi kukulitsa kumatako ndimanja pa matenda a kungambika kumatako pa chipatala cha UTH.

PACHIYAMBI; Dzina langa ndine Enock W. Soko, ndili pa maphunzilo pa sukulu ya university of Zambia. Phunzilo izachitidwa kuyesa kapena tingapeze njila zina zopoletsa matenda aya muziko ino. Motelo ndingakhale okondwa ngati mungatengapo mbali pa phunzilo iyi. Punzilo izatenga nthawi ma week 8. Otengapo mbala azaonedwa ku chipatalla pa ma week 2, 4 andi 6 itayambika chilitso. Ali yense otengapo mbali aza chilitsidwa ndi njila imodzi pa njila ziwili zimene zilinganizidwa. Mutundu wa kupoletsa uza patsiwa mosaembekezela. Kuti phunzilo iyi ikhale ndiphindu, onse otengapo mbali afunika kukonkha lamulo ya chilitso. Ndili okondwa kuti mwazipeleka kutengapo mbali pa phunzili iyi.

KUZI PELEKA NDIPONSO KULIPILIDWA; Onse otengapo mbali pa phunzilo iyi ndi ozipeleka. Ngati apezeka ndi vuto iliyonse poyetsa kuti opoletsedwe sadza patsiwa malipilo.

LINGO YA PHUNZILO; Kufuna kudziwa njila ya bwino panjila ziwili zo poletsa matenda yamene muli kudwala ya kuwawa kumatako.

PHINDU YO TENGAPO MBALI; Njila izi ziwili zikhoza kuchilisa matenda aya monga zoziwika kale. Potelo mungapeze thandizo potengapo mbali pa phunzili iyi, ndiponso anthu ena ambili angapezepo thandizo. Chipatala cha UTH nacho chikhoza kupezapo phindu.

Simuza patsidwa ndalama kapena zina zilizonse potengapo mbali.

CHIYOPEZO; Njila izi ziwili zopoletsa matenda aya zikhoza kukupatsani vuto yo wawa mutu, kuchotsa mphepo pa yokha ndiponso matuvi. Ngati izi zakuchitikilani, muza poletsedwa ndi njila zoziwika kale zamene zili pafupi.

KUCHINGILIDZA CHIYOPEZO; Ngati njila yopoletsela matenda ayo yalephela, njera zina zoziwika kale zizayetsedwa. Lingo niyakuti onse amene alikotengapo mbalii afunika kupoletsedwa. Mofuna kuchingiliza chiyopezo, njila zina zoziwika kale kupoletsa ziziyetsedwa. Ndipo onse afunikila kulembetsa zovuta zilizonse zimene aona pa njila yopoletsa. Koma ngati aona zobvuta kwambili, injila yopoletsa izaimitsidwa.

KUKANA KUTENGAPO MBALI; Ngati simufuna kutengapo mbali pa phunzilo iyi nikufuna kwanu. Ichi sichidza kuchingilizani kupedza thandizo ili yonse pa chipatala cha UTH. Ndiponso muloledwa kutsiya kutengapo mbali nthawi ili yonse mosapatsa chifukwa.

15.0 APENDIX IV: CONSENT FORM

TITLE OF STUDY: Randomised controlled trial comparing glycerine trinitrate treatment to manual anal dilatation in fissure in ano condition at UTH

DECLARATION: I have read / been explained to the context of the study and I fully understand the benefits and risks of participating. I therefore volunteer to take part with the understanding that I can withdraw from it at any time without facing any consequences.

Name of participant

Signed..... this..... day of.....20.....

Name of witness

Witness..... this..... day of.....20.....

Participant thumb print

Witness thumb print

NB: If you have any concern or questions not properly answered by the Doctor / nurse attending to you and you need clarification or to complaint, please get in touch with me Dr. Enock Soko, at UTH, Department of Surgery, cell 0977717477 or write to the address below.

University of Zambia (UNZA),
Biomedical Research Ethics Committee,
P. O. Box 50110,
LUSAKA
Tel: 256067

16.0 APPENDIX V: PEPALA YA CHIVOMEKEZO

MUTU WA PHUNZILO: Mosayembekezela Kulinganiza kuyesa Glycerine Trinitrate ndi kukulitsa kumatako ndimanja pa matenda a kungambika kumatako pa chipatala cha UTH

Kulankhula : Nawelenga kapena anifotokozela za phunzilo iyi ndipo ndikuti namva phindu ndiponso ziopyezo zinga chitike potengapo mbali. Motelo nizipeleka kutengapo mbali malinga ndinga leke kutengapo mbali nthawi iliyonse mopanda zolondolola.

Dzina langa;.....

Sign;..... iyitsiku ya20.....

Mboniiyi tsiku ya20

Zanja ya otengapo mbali

Zanja ya mboni

Zdzina : Ngati muli nachikaiko kapena muli na funso yamene siinayankhiwe bwino ndi a dokota kapena a nasi, onani ine Dr Enock Soko pachipatala cha UTH ku gawo ya surgery kapenanso tumani lamya pa 0977717477. China nichakuti lembani kalata ku keyala iyi;
University of Zambia,
Biomedical Research committee,
P.O.Box 50110,
LUSAKA
Tel: 256067