

Dissertation

**“COMPARATIVE STUDY OF BOTULINUM TOXIN INJECTION AND
LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT
OF CHRONIC ANAL FISSURE”**

Dissertation submitted to

**THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY
CHENNAI**

in partial fulfilment of the regulations for the Award of the degree of

M.S. (General Surgery)

Branch – I



**THE TAMIL NADU Dr. M.G.R. MEDICAL UNIVERSITY
CHENNAI**

May 2020

Registration Number: 221711005

CERTIFICATE

This is to certify that, the dissertation entitled “**COMPARATIVE STUDY OF BOTULINUM TOXIN INJECTION AND LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT OF CHRONIC ANAL FISSURE**”

Is the bonafide work done by **DR. CHETNA RAVINDRA**, with Registration Number: **221711005** during her **M.S. (General Surgery)** course **2017-2020**, done under my supervision and is submitted in partial fulfilment of the requirement for the **M.S.(BRANCH-I)- General Surgery** of The Tamil Nadu Dr.M.G.R. Medical University, May 2019 examination.

Prof. Dr. R. KANNAN M.S.,

Director
Institute of General Surgery
Madras Medical College
Chennai – 03.

Prof. S.MANISELVI M.S., DGO.,FICS

Professor
Institute of General Surgery
Madras Medical College
Chennai – 03.

DR. R. JAYANTHI M.D., FRCP,

THE DEAN

Madras Medical College &
Rajiv Gandhi Government General Hospital
Chennai-03

DECLARATION

I, certainly declare that this dissertation titled “**COMPARATIVE STUDY OF BOTULINUM TOXIN INJECTION AND LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT OF CHRONIC ANAL FISSURE**” represents a genuine work of mine. The contributions of any supervisors to the research are consistent with normal supervisory practice, and are acknowledged.

I also affirm that this bonafide work or part of this work was not submitted by me or any others for any award, degree or diploma to any other University board, either in India or abroad. This is submitted to The Tamil Nadu Dr. M.G.R. Medical University, Chennai in partial fulfilment of the rules and regulations for the award of Master of Surgery Degree Branch I (General Surgery).

DATE:

DR. CHETNA RAVINDRA

PLACE:

(POST GRADUATE)

ACKNOWLEDGEMENTS

The practice of surgery can be learned from teachers, by years of training, and regular honing of skills obtained. However, research is essential for the betterment of the art of surgery. Without research any new knowledge is just that- it cannot become an actualization. Through this study, I'd like to contribute my little to the research world, with the help of those who have been a guiding light throughout my quest of surgical education.

With immense pleasure, I would like to thank my respected Professor and guide for this dissertation Prof. Dr. S.Maniselvi M.S, D.G.O, for her invaluable guidance. She has been an academic, psychological and moral support throughout my postgraduation period. Her continuous dedication to patient care and teaching have been an inspiration. At every step of this study, she was with me motivating towards improvement.

I wish to extend a deep sense of gratitude to the Director of Institute of General Surgery, Prof. Dr. R. Kannan M.S, for his constant guidance, help and encouragement.

My assistant professors – Dr. D. Manivannan M.S, Dr. D. Vinodh M.S and Dr. T. Paulia Devi M.S have been at the helm of my surgical education. They have been instrumental in not only teaching me the basics of surgery, different surgical techniques but also in inculcating the interest to read, train and research extensively. Every single day spent with them has been an enriching experience.

I thank the Dean, MMC & RGGGH for support and permitting me to conduct this study.

Many thanks to the ethical committee for sparing their valuable time to review and kindly permitting my research.

I also thank my fellow postgraduates, and colleagues who have extended their co - operation in my work.

I would be failing in my duty if I do not appreciate all the patients who have helped me to become a surgeon. A special thanks to the patients who consented to be part of this study. Many thanks to the anesthetists involved in this study for their cooperation.

Finally, I would love to thank my parents who have been supportive of me throughout my journey and for always being there.

LIST OF ABBREVIATIONS

IAS	Internal Anal Sphincter
EAS	External Anal Sphincter
BTX	Botulinum Toxin
POD	Post Operative Day
SNOSE	Sequentially Numbered Opaque Sealed Envelope

TABLE OF CONTENTS

ABSTRACT	8
INTRODUCTION	9
AIMS AND OBJECTIVES	11
REVIEW OF LITERATURE	12
MATERIALS AND METHODOLOGY	41
RESULTS	51
DISCUSSION	70
CONCLUSION	73
REFERENCES	74
ANNEXURE 1: LIST OF FIGURES	78
ANNEXURE 2: LIST OF TABLES	79
ANNEXURE 3: INFORMATION SHEET	80
ANNEXURE 4: PATIENT CONSENT FORM	82
ANNEXURE 5: QUESTIONNAIRE	83
ANNEXURE 6: ETHICAL COMMITTEE APPROVAL	85
ANNEXURE 7: PLAGIARISM CERTIFICATE	86
ANNEXURE 8: MASTER CHART	89

ABSTRACT

Aims:

Chronic anal fissure is a commonly seen, painful condition, which may require surgery. This study determines if Botulinum toxin injection can replace lateral internal sphincterotomy as treatment for the disease.

Methods:

This study- a randomised controlled trial included 60 patients. They were randomly divided into two groups, one half received Botulinum toxin injection and the other half underwent lateral internal sphincterotomy surgery. They were then followed up over a period of 3 months and data collected regarding relief of pain, return to daily activities, healing of fissure, wound infection, incontinence and recurrence.

Results:

Results showed that Botulinum toxin injection showed faster pain relief (40% vs 6.7% at day 1) and earlier return to daily activities when compared with surgery (mean: day 2 vs day 4). There was no significant difference between the two with respect to healing of fissure, wound infection and recurrence. However, incidence of incontinence was higher in the surgery group (10% vs 3.3%).

Conclusion:

Botulinum toxin injection can be considered as a suitable alternative to lateral internal sphincterotomy with advantage of being a quick and easy technique as well as causing less morbidity.

Keywords

Fissure, Botulinum toxin, Lateral internal sphincterotomy

INTRODUCTION

Fissure-in-ano is a very commonly seen condition daily in the surgical outpatient department.

A fissure in ano is a tear in the anoderm distal to the dentate line.

The pathophysiology of anal fissure is associated with trauma from either the passage of hard stool or prolonged diarrhea. This causes a tear in the anoderm, subsequently leading to spasm of the internal anal sphincter. Pain and increased ischemia contribute to the development of a poorly healing wound that becomes a chronic fissure.

85 to 90% of fissures occurs in posterior midline. 10 to 15% occur in anterior midline. Less than 1% occur off midline.¹

First-line therapy of anal fissure includes bulk agents, stool softeners and warm sitz baths. Analgesic creams, nitroglycerin creams, diltiazem ointments have also been used to heal fissures. Medical therapy is effective mostly in acute fissures but fails to treat chronic fissures.

Surgical therapy is recommended for chronic fissure and lateral internal sphincterotomy is the procedure of choice. The objective of this procedure is to decrease the spasm of the internal sphincter by dividing a portion of the muscle. Approximately 30% of the fibres are divided laterally.

Chronic fissures are usually treated surgically with division of spasmodic internal anal sphincter. Usual period of healing of the fissure is over 1- 3 months post the surgery. Around 5-15% of the patients suffer from permanent sphincter damage in the form of incontinence to either flatus or feces.

Hence there was a need to find different methods which prevent the morbidity of the surgical technique and chemical sphincterotomy was enunciated.

Botulinum toxin is one such method. It acts by preventing acetylcholine release from presynaptic nerve terminals causing temporary muscle paralysis.

Identification of an alternative treatment modality, such as injection of botulinum toxin into the internal anal sphincter can be helpful in avoiding surgical intervention and may be used interchangeably or as a possible replacement.

AIMS AND OBJECTIVES

To compare injection of botulinum toxin in the anal sphincter with the gold standard treatment for chronic fissure in ano- lateral internal sphincterotomy in terms of:

- Efficiency of treatment

Measured by the relief of pain, rate of healing of fissure and by ease of return to work

- Occurrence of complications

Such as wound infection and incontinence

- Recurrence rates

And thereby determine if botulinum toxin can be a replacement for surgical sphincterotomy.

REVIEW OF LITERATURE

The anal canal is the terminal end of the 9 metre long alimentary canal. It begins at the anorectal junction and ends at the anal verge. The puborectalis muscle acts like a sling, pulling on the anorectal junction producing an anorectal angle of 90-100°.

Anal canal consists of the following structures:

- Inner epithelial lining
- Vascular subepithelium
- Anal sphincters- internal and external
- Fibromuscular supporting tissue
- Dense neuronal network- autonomic and somatic

At rest, the length varies from 2.5 to 5 cm, forming an oval slit in the anteroposterior plane, rather than a cylindrical canal.¹

Anteriorly, perineal body is present. This is attached to the middle third of the anal canal via dense connective tissue. Laterally and posteriorly, the anal canal is surrounded by loose adipose tissue, allowing expansion while passing stools. Posteriorly, anococcygeal ligament connects it to the coccyx.

Interior of the Anal Canal

The interior of the anal canal can be divided into 3 parts

Upper Mucous Part

This part is the first 15 mm is lined by columnar epithelium, similar to that of rectum. It contains secretory cells, with numerous tubular glands or crypts. 6 to 10 vertical folds called

the anal columns of Morgagni are present. Each of them has a terminal radicle of the superior rectal artery and vein. These are largest in the left median, right anterior and right posterior regions, where the subepithelial tissue expands to form anal cushions. Anal cushions help in the maintenance of continence to both flatus and feces.

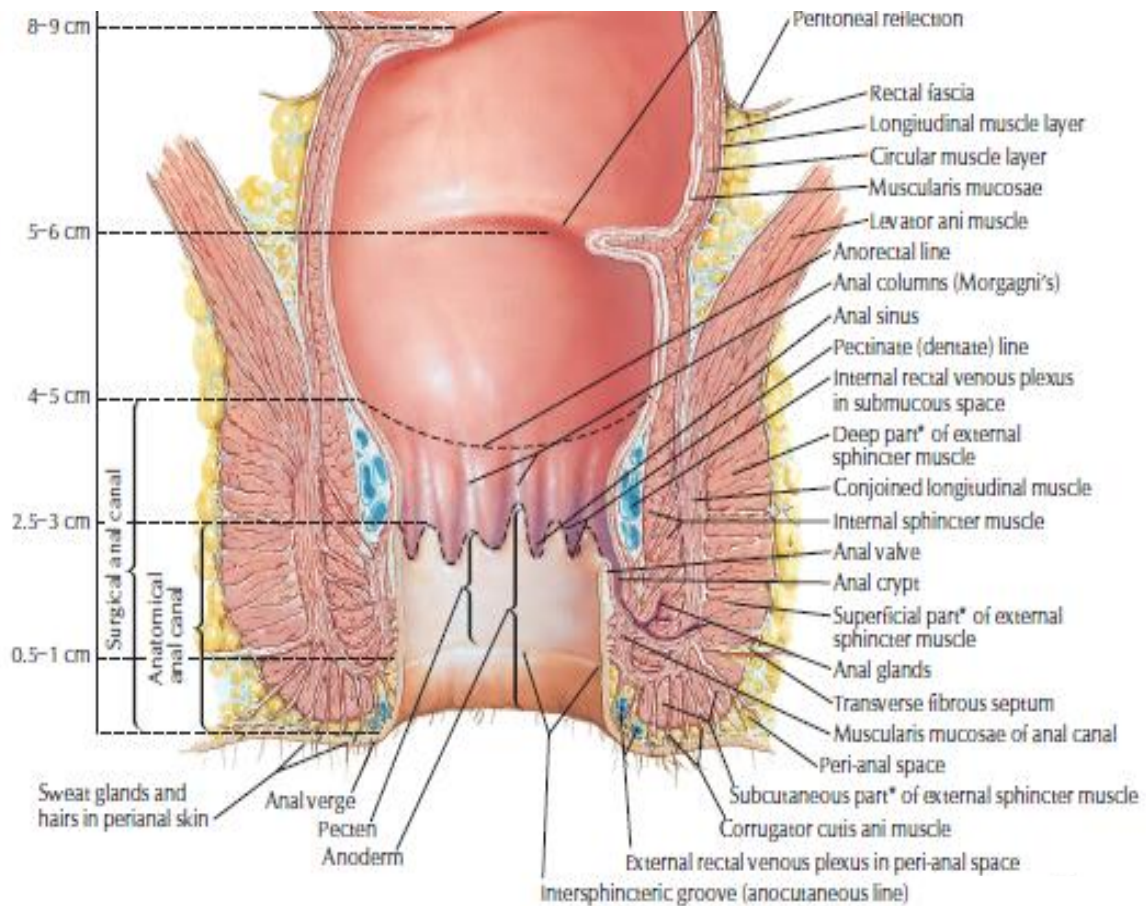
The lower ends of the anal columns are joined together by short transverse folds of mucous membrane; these folds are called the anal valves, which lie in between recesses called the anal sinus. Anal glands open into anal crypts within the anal valves. The anal valves and sinuses together form a transverse line - the pectinate line. It is situated at the level of the middle of internal anal sphincter and is considered the junction of ectodermal and endodermal parts.

Middle Part

Also called as transitional zone or pecten, this region is also lined by non-keratinized stratified squamous epithelium, which is devoid of sweat glands, but rich in somatic nerve endings. The epithelium is thin and pale- the venous plexus is visible through. The lower border of the pecten is marked by the White line of Hilton. It is situated at the level of the interval between the subcutaneous part of external anal sphincter and the lower border of internal anal sphincter.

Lower Part

It is lined by keratinized stratified squamous epithelium with sweat and sebaceous glands, which is continuous with perianal skin.



*Parts variable and often indistinct

Figure 1: Anatomy of Anal Canal

Anal Sphincters

Internal Anal Sphincter

Continuous with the circular muscle of the rectum, it is a well defined ring. Smooth muscle fibres are oriented obliquely terminating at the junction of subcutaneous and superficial parts of the external sphincter. Its thickness varies between 1.5 to 3 mm.¹ The lower portion of the IAS (internal anal sphincter) has fibres from the conjoint longitudinal coat of the rectum, strands of which pass into the submucosa.

Blood Supply – terminal branches of superior rectal vessels and branches of inferior rectal vessels.

Innervation – Sympathetic fibres originate from lumbar spinal segments L4 and L5, distributed via inferior hypogastric plexus and cause contraction of the sphincter. Parasympathetic fibres originate from sacral plexus, are also distributed via inferior hypogastric plexus and cause relaxation of the sphincter.

External Anal Sphincter

It is a tube like complex of striated muscle. The type of muscle fibre in this is type 1 or the slow twitch skeletal muscle fibre which are involved in prolonged contraction. It is divided into three parts- subcutaneous, superficial and deep. However, the external anal sphincter acts like a single anatomical and functional entity. The fibres of the EAS decussate with surrounding muscles such as the superficial transverse perinei, perineal body anteriorly; and the anococcygeal raphe posteriorly.

Blood Supply – terminal branches of the inferior rectal vessels with a small contribution from the median sacral artery.

Innervation – Main supply is from the inferior rectal branch of the pudendal nerve (anterior division of S2, S3, S4).

Between the two sphincters is a layer called longitudinal coat, having two components. Conjoint longitudinal coat is a fibroelastic-muscular layer which throws multiple septae into the perianal space and helps form the intersphincteric groove. The second component is intersphincteric space connective tissue.

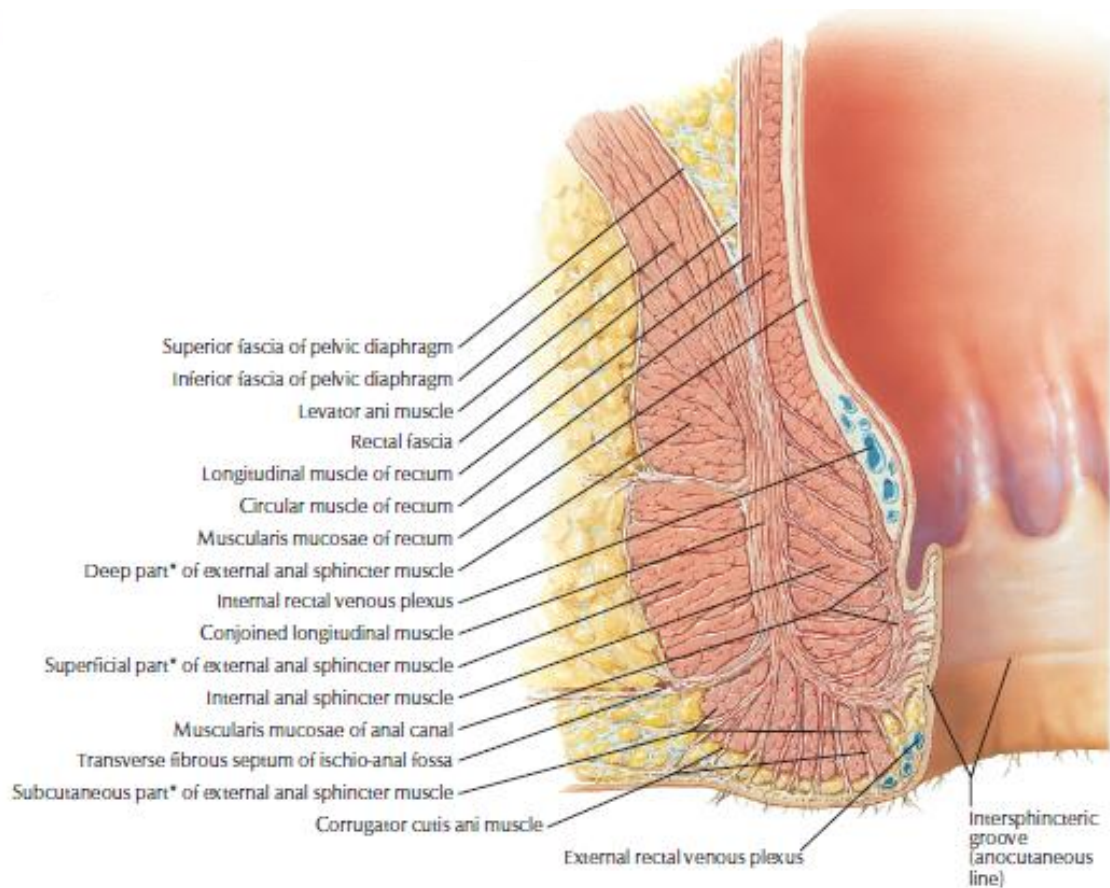


Figure 2: Anatomy of Sphincters

Innervation of the Anal Canal

Anal Canal is innervated by both autonomic and somatic nervous systems.

Preganglionic sympathetic fibres originate from lower two lumbar segments. They run via the lumbar sympathetic chain into sacral ganglia and then via the sacral splanchnic nerves into the inferior hypogastric plexus.² Parasympathetic fibres originate in the second to fourth sacral spinal segments; run to the inferior hypogastric plexus via pelvic splanchnic nerves.

Postganglionic fibres of both run together in nerves of pelvic plexus and enter lower rectal wall via the lateral ligaments of the rectum and anorectal junction.

Sympathetic fibres cause, via the α -adrenergic receptors

- Relaxation of the lower rectal muscle
- Contraction of the conjoint longitudinal coat and internal sphincter

Parasympathetic fibres cause, via the muscarinic receptors

- Relaxation of the internal sphincter
- Release of nitric oxide from nitrergic neurons.

Somatic innervation is via anterior divisions of second to fourth sacral spinal nerves through the inferior rectal branch of pudendal nerve. They supply the external sphincter, the lower half of mucosa and the perianal skin.

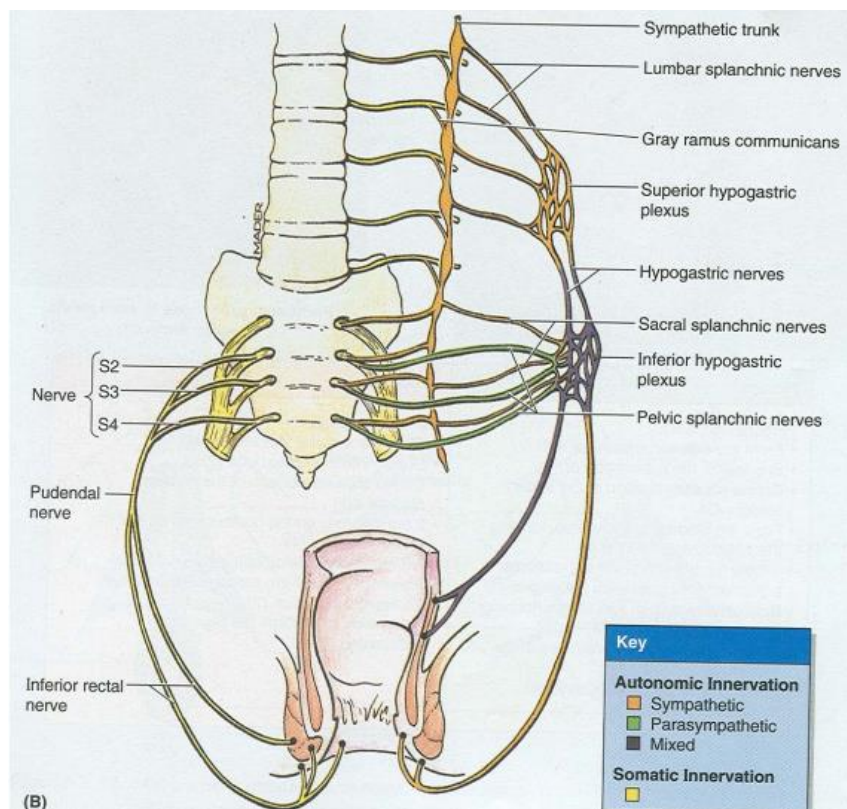


Figure 3: Innervation of Anal Canal

Pain in the lower thirds of the anal canal is referred around to the perineum also.

Anorectal intramural plexus and sacral spinal cord help in reflex arc help in anorectal function.

Initiation of defecation needs complete coordination of lower rectum and the two sphincters.

Whenever there is rectal distension due to stools, there is a reflex relaxation of the internal sphincter. This is called as Recto-Anal Inhibitory Reflex or RAIR. Neural activity regulates:

- Defecation
- Separation of feces from rectal gas
- Local adjustments to fecal consistency
- Self cleansing movements in rectum and anal canal
- Coordination with other musculature of perineum

The anal canal is kept closed by maintaining a higher pressure in anal canal than in the rectum. This resting pressure is maintained by high tonic pressure of the internal anal sphincter. A sudden increase in intra-rectal pressure such as during coughing or exertion is combated by spinal reflex causing contraction of puborectalis and external sphincter.

Defecation is a response to feeling the need to pass stool stored in rectum. It a conscious physiological act. Mass colonic contractions drive feces into rectum, which slowly distends. Entrance of feces into the upper anal canal activates mucosal receptors. A conscious contraction of external sphincter can be done at this stage. This causes ceasing of contractions, followed by retrograde peristalsis.

Initiation of defecation starts with conscious relaxation of the pelvic floor muscles so that the pelvic floor descends slightly. The anorectal angle then becomes straight. External anal sphincter is voluntarily relaxed. This causes reflex relaxation of internal anal sphincter and conjoint longitudinal coat. Anal canal now stands in an open position. Abdominal muscles contraction further raises intrabdominal pressure and defecation occurs.

Standard anorectal manometry is used to measure intrarectal pressure. Manometry catheters contain multiple lumens at equidistant spaces such as 1 cm and are constantly water-perfused.² After preparation with a saline enema, insertion of the catheter into the rectum, maximal resting pressure and maximal squeeze pressure are measured. Resting pressure is measure by stationary pull through. Average resting pressures in normal individuals is 40 – 80 mm Hg. Squeeze pressure is the pressure recorded by voluntary squeezing of the anal canal for 5 seconds without contacting abdominal muscles. Average values for normal individuals is 80-160 mm Hg.³

Resting pressure is mostly contributed to by Internal Anal Sphincter (85%) and partially by External Anal Sphincter (15%). Squeeze pressure is contributed to completely by the External Anal Sphincter.⁴

Fissure in-ano

Anal fissure is described as a linear defect, or laceration, in the anoderm, located between the dentate line and the anal verge. An acute fissure is a simple laceration, whereas a chronic anal fissure is an ulceration with built-up scarred edges and exposed internal anal sphincter muscle fibers at its base. ⁵

Additional findings may include

- Perianal skin tag at the external margin of the fissure
- Hypertrophied papilla at the dentate line
- Visible muscle

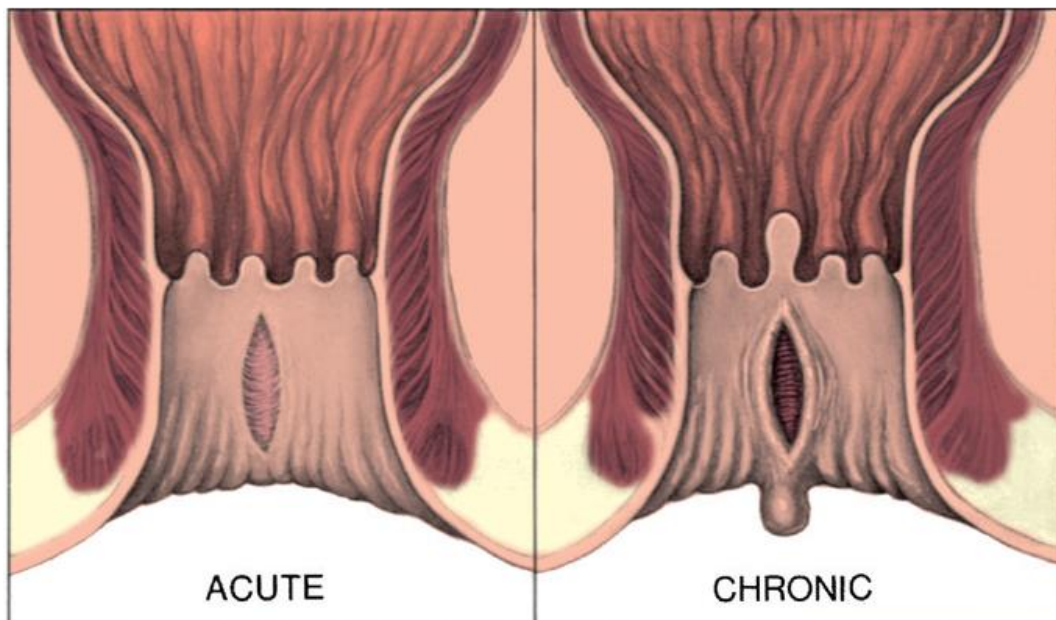


Figure 4: Acute vs Chronic fissure

It is a common condition that usually presents as anal pain or bleeding with defecation. Bleeding is usually scant, bright red, and found on the tissue when cleansing after a bowel movement.

Etiology

- Passing hard stools causing trauma, is the most common.
- Frequent passage of loose watery stools
- Preexisting anal canal irritation.
- Scarring, stricture, and stenosis, from prior anal injury or surgery
- Infections- Syphilis and Tuberculosis.
- Sexually Transmitted Diseases and Infections associated with immunocompromised conditions chancroid, herpes simplex virus, and cytomegalovirus causing atypical anal canal ulcers.
- Systemic conditions that are associated with atypical anal fissure/anal ulcer are Crohn's disease and Acquired Immunodeficiency Syndrome. ⁶

Acute and chronic anal fissures are almost always located in the midline with the posterior location of 6 o'clock predominating (women, 90%; men, 99%). ¹

Atypical features include

- fissures at non-midline positions,
- large shaggy fissures,
- defects with undermined edges, or
- granulation tissue in the base.

Actual cavitation of the internal sphincter is another ominous clue to the presence of systemic disease. A fissure or an ulcer with a mass should raise the suspicion of malignancy. Lymphoma, leukemic ulcer, and anal canal epithelial tumors are often associated with surface defects.⁷

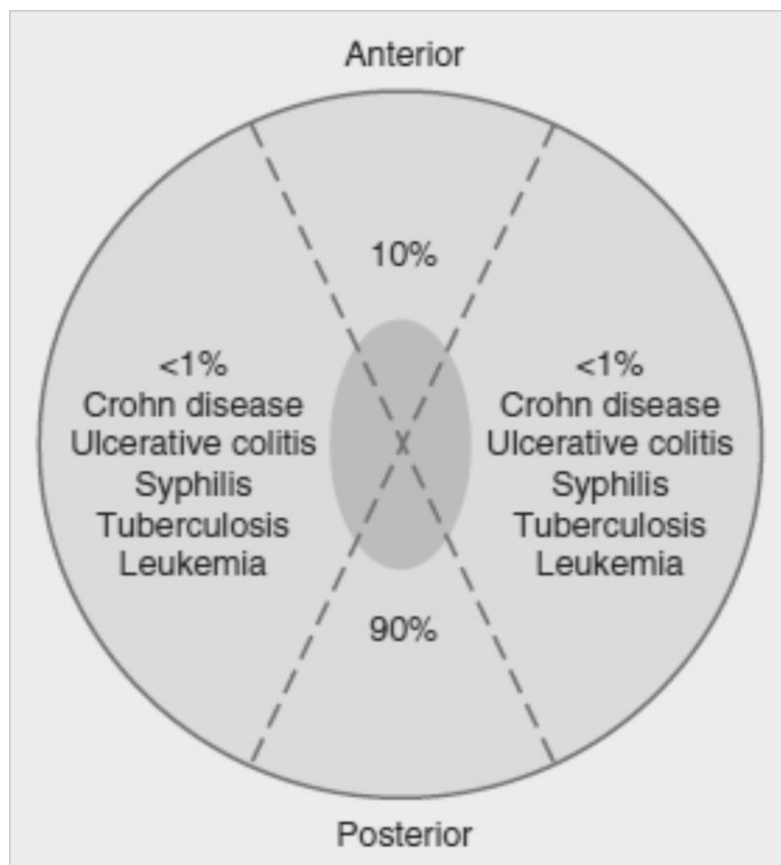


Figure 5: Etiology of fissure in ano

Theories regarding fissure in ano

- Klosterhalfen et al, in 1989 reported on the blood supply of the inferior hemorrhoidal artery. In the 85% of cadaver specimens, the posterior commissure of the anal canal was not directly perfused except by end arterioles. ⁸

Branches of these sphincteric arterioles occurred at right angles and coursed perpendicularly through the circular fibers of the internal sphincter. This alerted towards the possibility of decreased mucosal perfusion, particularly in the posterior midline. Moreover, sphincter spasm and hypertonicity, may further decrease blood flow posteriorly.

- Schouten et al, have shown increased anal canal pressures correlated with decreased mucosal blood flow as measured by Laser Doppler flowmetry. ^{9,10}

Hence in chronic anal fissure, the decreased blood flow further delayed the healing of fissure.

Presenting Complaints

- Tearing or burning pain during defecation
- Pain lasts few minutes to hours
- Feeling of tightness or spasm
- Bleeding per rectum- usually blood lined over stool
- Passing of scant or hard pellet like stools
- Pain causes further constipation, which then aggravates fissure- forming a vicious cycle

Examination needs to be carefully performed. Local anesthetic is not very useful while examining and digital insertion or endoscopy is contraindicated. Simple spreading of the buttocks is done to gently roll open the anal verge and demonstrate the fissure.

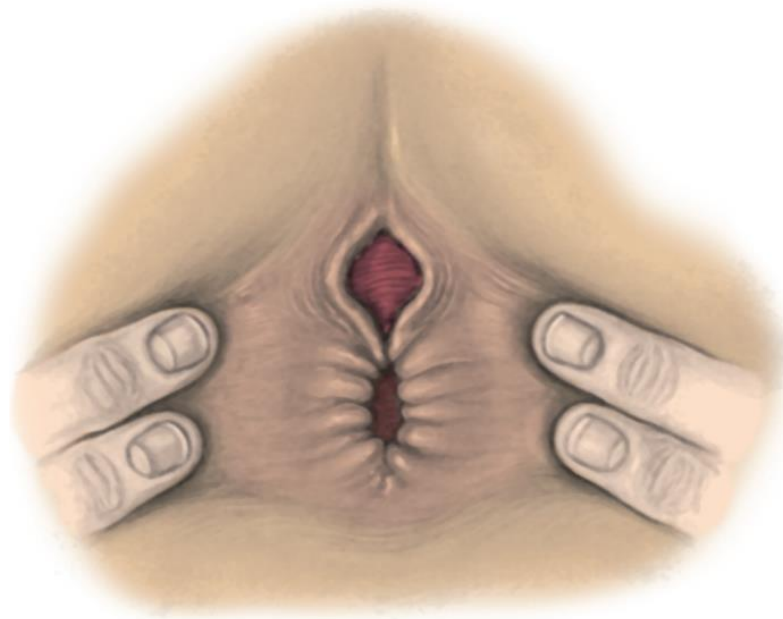


Figure 6: Examination of anal fissure

Sphincter spasm is common in chronic anal fissure. Resting pressure are found to be as high as 90-120 mm Hg. It is the spasm of the internal sphincter which causes formation of the hypertrophied papilla covering the fissure.

Treatment

The first line of treatment for acute fissure in ano includes

- Warm-water sitz baths.

Local heat helps in relief of pain. The patient is advised to buy a tub in which warm water is filled. Rock salt, povidone iodine can be added. A randomized controlled trial study conducted by Gupta in 2006 showed that while sitz bath helped in patient satisfaction, there was no statistical benefit when used in patients having fissure in ano.¹¹

- Stool-bulking agents.

Psyllium, bran, and fibre, draw water into the stool, changing its consistency, preventing the formation of hard stool that causes sustained trauma to the anal canal.

Conservative, nonsurgical measures successfully heal 90% of acute anal fissures, but only 40% of chronic fissures.¹²

Nitroglycerin

Improving the blood supply and relaxing the sphincter facilitate healing of anal fissure. Nitric oxide is a potent smooth muscle relaxant and promotes vasodilation. Topical nitroglycerin is absorbed transcutaneously. It acts by releasing nitric oxide. When applied to the anus, reduces anal canal pressure. It is used in patients having fissures that do not heal with stool-bulking agents and local heat therapy, as a second line measure. Multiple randomized controlled trials conducted have shown nitroglycerin to be significantly more effective than a placebo.¹²



Figure 7: Nitroglycerin ointment

0.2% or 0.4% cream is used twice daily using a Q-tip. Nitroglycerin should be protected from air and light, a pea sized amount (200 -500 mg) is applied to the anal verge. Pain relief is immediate and lasts upto 12 hours. The significant adverse effect is headache, due to dilatation of cerebral vasculature. Others are syncopal attacks, postural hypotension. Healing of fissure takes 4-6 weeks. Recurrence rates are high. Retreatment can be done with the same medication.

Richard et al in 2000, compared after randomization nitroglycerin and internal sphincterotomy. Nitroglycerin group has less than 50% treatment rate at 2 months, high incidence of headaches as an adverse effect.¹³ They also found that patients who did have a cure, also had a very high recurrence rate. The major problem was the discontinuity of treatment due to headache. Thus, there is a problem with compliance with this method.

Nifedipine and Diltiazem

Calcium channel blockers such as nifedipine and diltiazem have also been found to be effective by reducing resting anal sphincter pressures. Topical 2% diltiazem, is as effective as nitroglycerin in the treatment of chronic anal fissures. In fact, topical diltiazem heals also heals upto 75% of fissures that have failed to heal with nitroglycerin alone. The main advantage is reduced incidence of side effects as compared to nitroglycerin.

Knight et al studied the effectiveness of Diltiazem in patients with fissure in ano and found to have complete treatment in 2 months in about 75% of patients.¹⁴ Rest of the patients needed prolonged treatment. Compliance rates were very good due to very few adverse effects. Just one of 75 patients studied complained of headache and 3 of perianal dermatitis.



Figure 8: Diltiazem ointment

Surgical Treatment

Lord's dilatation was one of the earliest methods used to relax the sphincter. It is done under general anesthesia using four fingers of each hand to cause vigorous stretching of the anal canal. This usually breaks the circular constricting band in the anorectum, but sometimes may cause a tear in the levator ani as well.

Two studies done showed the incidence of loss of sphincter ton to be as high as 13%. There was also a failure of treatment in anal fissure, with less than 40% having relief of symptoms in 6 month follow up period.¹⁵ Endosonographic studies have shown destruction of anal sphincter in more than 50% of the patients undergoing this procedure, with most of the patients having permanent damage being females.¹⁵

Stretching of the anal sphincters using two fingers of each hand described by Recaimer in 1829 was an alternative.

Dilation of the anal canal by finger insertion technique has fallen out of favor and should be discouraged because this procedure stretches the anal canal in an uncontrolled fashion resulting in unacceptable levels of postoperative incontinence.¹⁶

Retractors and balloon-tipped dilating catheters have been used for dilation in the treatment of chronic anal fissures.

Sphincterotomy

The first sphincterotomy was done by Brodie in 1839. However, the structure divided was not identified. It was first described by Eisenhammer in 1951.¹⁷ The strategy of sphincterotomy is to divide the hypertonic portion of the internal anal sphincter muscle to reduce anal canal

pressure and facilitate healing of the anal fissure.¹⁸ However long term follow up showed problems of delayed healing with the formation of a keyhole deformity due to this surgery.

Keyhole deformities are persistent grooves in the midline following sphincter division that may result in anal seepage or incontinence. This procedure was modified by repositioning the incision to the right or left lateral position. This was found to prevent the occurrence of the deformity.^{19,20}

Two types of sphincterotomy are described now. In open method, skin is incised laterally for about 2 cm at 3 or 9 o'clock position, free edge of the internal sphincter is dissected and about 1/3rd is divided. Wound may be left open to granulate or can be closed using absorbable sutures. Post operative complications include bruising, hematoma, perianal abscess, fistula and incontinence.²¹

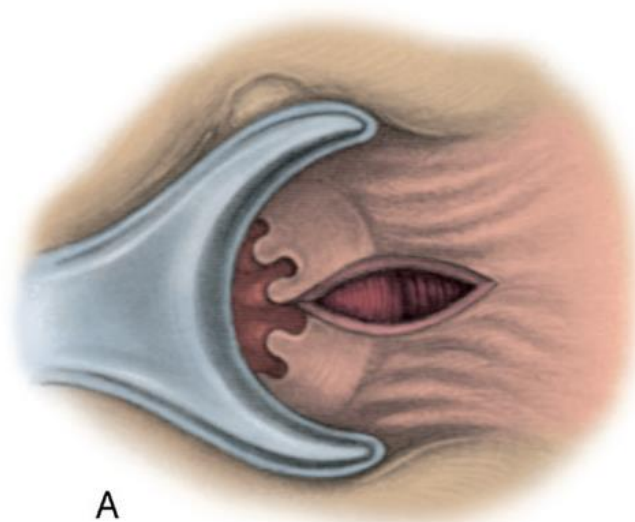


Figure 9: Lateral Open Sphincterotomy- incision

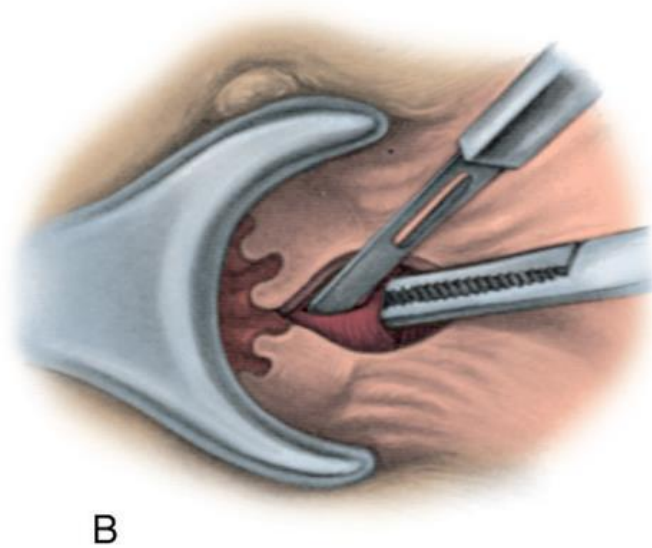


Figure 10: Dissecting internal sphincter fibres

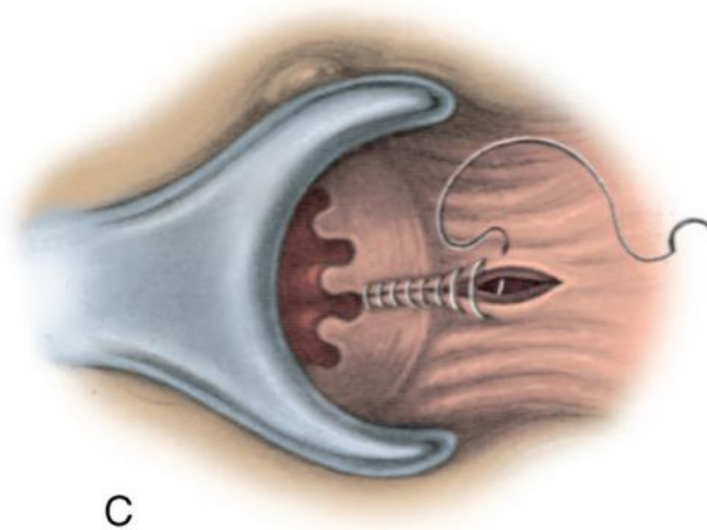
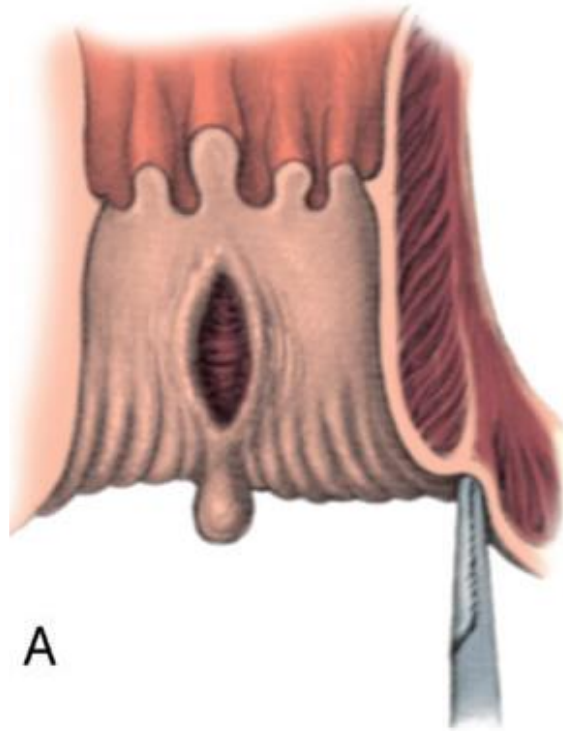


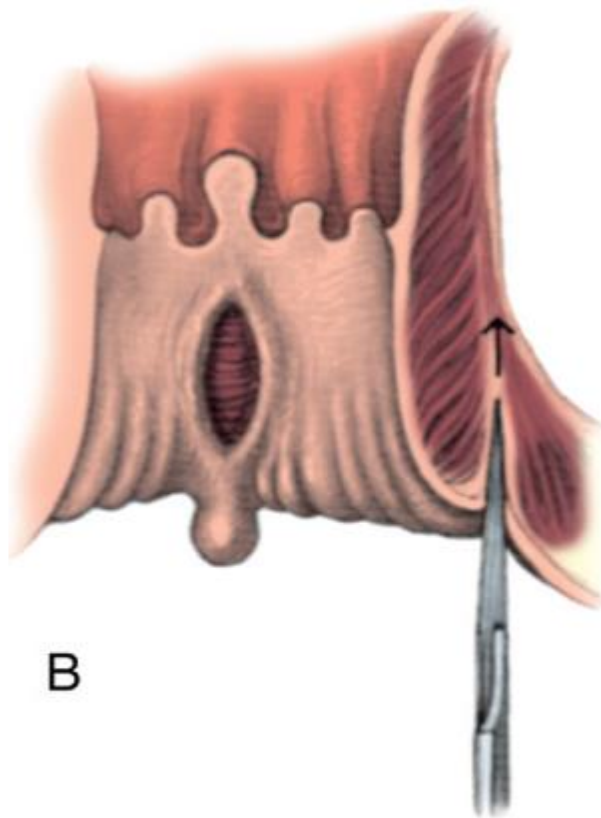
Figure 11: Fibres cut and wound closed if needed

Notaras introduced the closed sphincterotomy that is performed through a stab incision at the intersphincteric groove rather than an open exposure of the internal sphincter.²² A '11' blade is introduced in the groove facing upwards and then rotated medially to cut the fibres.



A

Figure 12: Lateral Closed Sphincterotomy



B

Figure 13: 11 blade inserted at groove

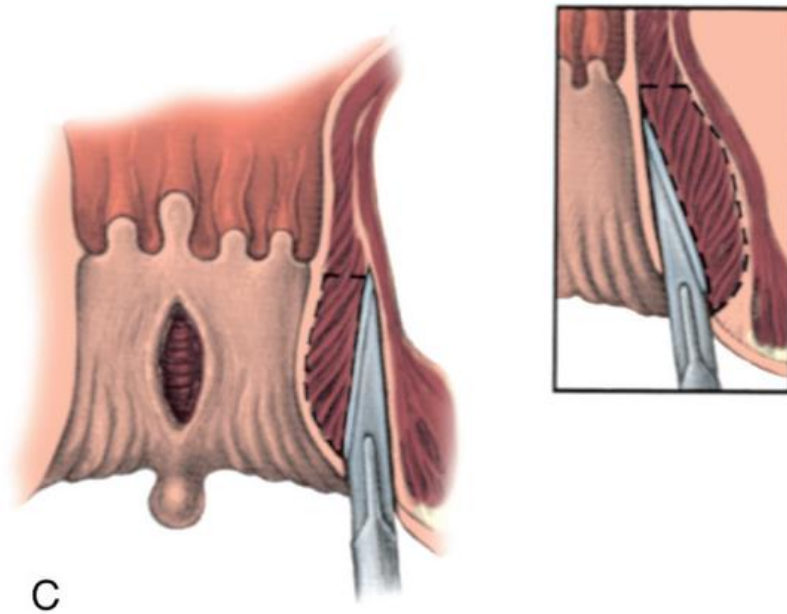


Figure 14: Blade rotated through fibres

Fissurectomy is done by excising the entire fissure and sentinel pile via an elliptical incision. The transverse lower fibres of internal sphincter are divided in the floor of the fissure.^{23,24} The specimen is sent for biopsy to rule out malignancy, Crohn's, tuberculosis etc.

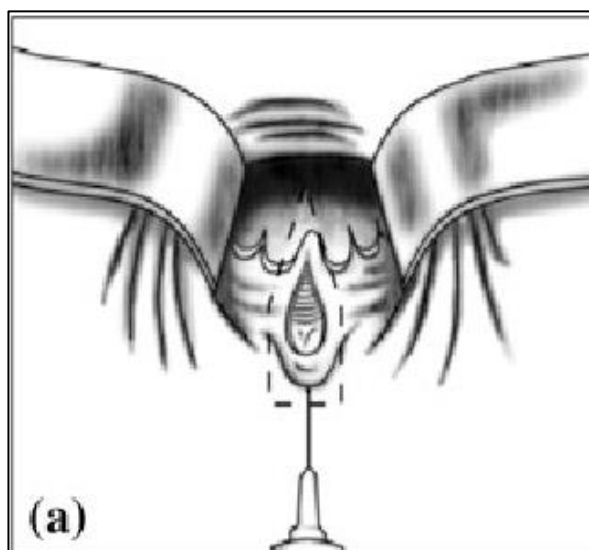


Figure 15: Excision of fissure

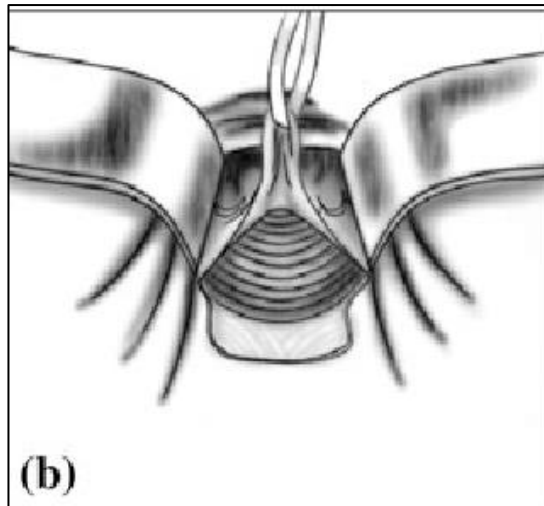


Figure 16: Raising of mucosal flap

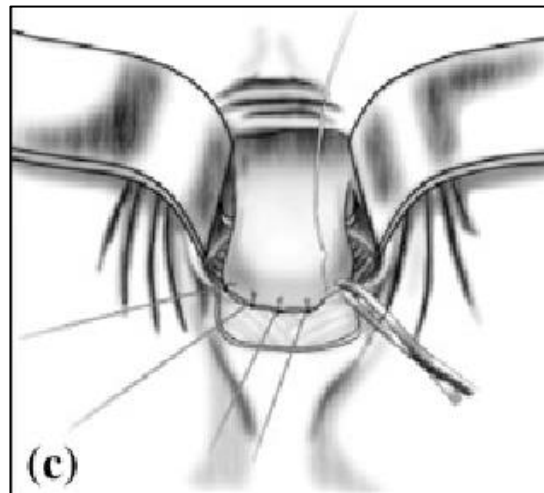


Figure 17: Closure by mucosal flap (optional)

Any fissure which is atypical, should be subjected to biopsy keeping in mind a high suspicion for the differential diagnoses.

Colonoscopy may be offered in such cases to rule out underlying pathology. Blood tests should be done to rule out sexually transmitted diseases. Treatment of the underlying causes helps in the treatment of such fissures. Regular treatment for anal fissure is usually not done in such patients.

A meta-analysis by Nelson analysed 17 publications retrospectively. Operative techniques commonly used for fissure-in-ano include anal stretch, open lateral sphincterotomy, closed lateral sphincterotomy, posterior midline sphincterotomy were compared from these studies by assimilating all data.

2,727 patients were involved. Significant differences were found for recurrence among all the methods of surgery except anal stretch. Incontinence to flatus was higher in anal stretch compared to all forms of sphincterotomy.²⁵ No significant difference was found comparing open to closed lateral internal sphincterotomy for persistence of fissure or incontinence. Posterior midline sphincterotomy was not significantly different from lateral sphincterotomy related to persistence or incontinence.

Botulinum Toxin

Neurotoxin produced by *Clostridium botulinum* is one of the most potent toxins known. 7 toxin serotypes are present- BTX- A, B, C, D, E, F, AND G. Of these all affect human nervous system except BTX- C and D. ²⁶

Potential medical applications of Botulinum toxin were first discovered by Scott in 1980s when he locally injected minute quantities for the treatment of strabismus, leading to its approval for the usage in strabismus, hemifacial spasm and cervical dystonias. ²⁷

Botulinum toxin is produced as an inactive chain of 150 kD, which is then cleaved into a dichain peptide, comprising of heavy and light chains, both of which are required for toxicity.

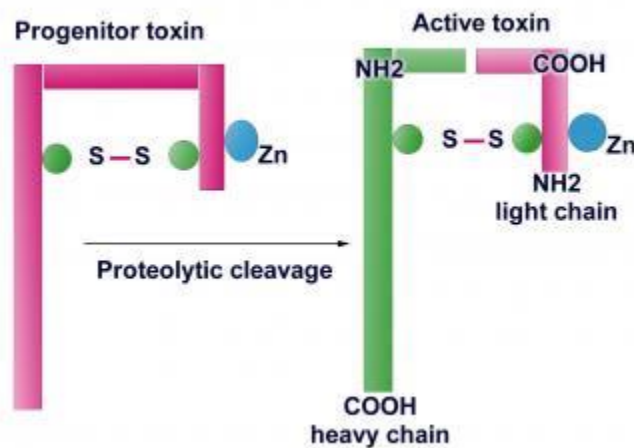


Figure 18: Botulinum toxin molecule

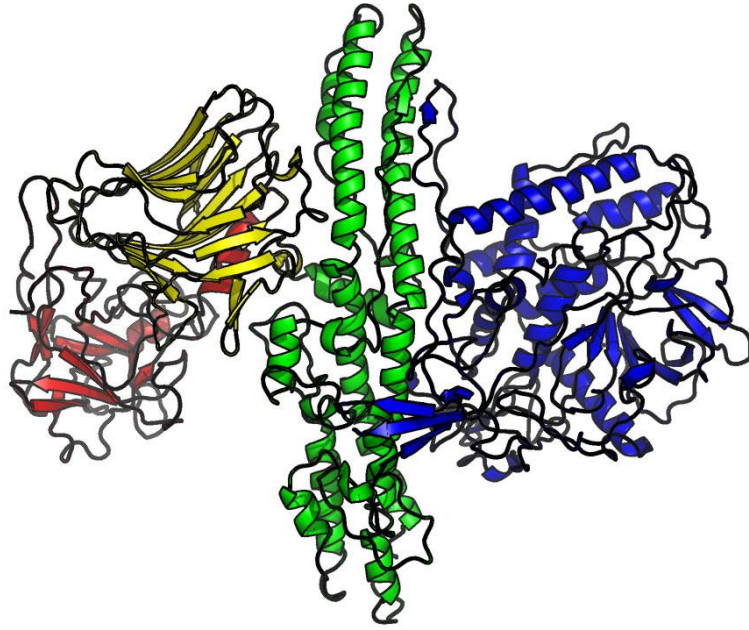


Figure 19: Molecular pattern of Botulinum toxin

Blue part represents light chain

Green represents heavy chain

Mechanism of Action

Botulinum toxin acts by inhibiting release of acetylcholine in presynaptic terminal of neuromuscular junction. The first step is irreversible binding to the presynaptic cholinergic receptors via H chain, called synaptotagmin.²⁸ Next, the toxin is internalized by receptor mediated endocytosis. H chain helps in formation of an ionic channel and L chain is transmitted from endosome into the cytoplasm. Botulinum toxin type A then cleaves SNAP 25 (synaptosomal associated protein). This prevents docking and hence, the release of acetylcholine.

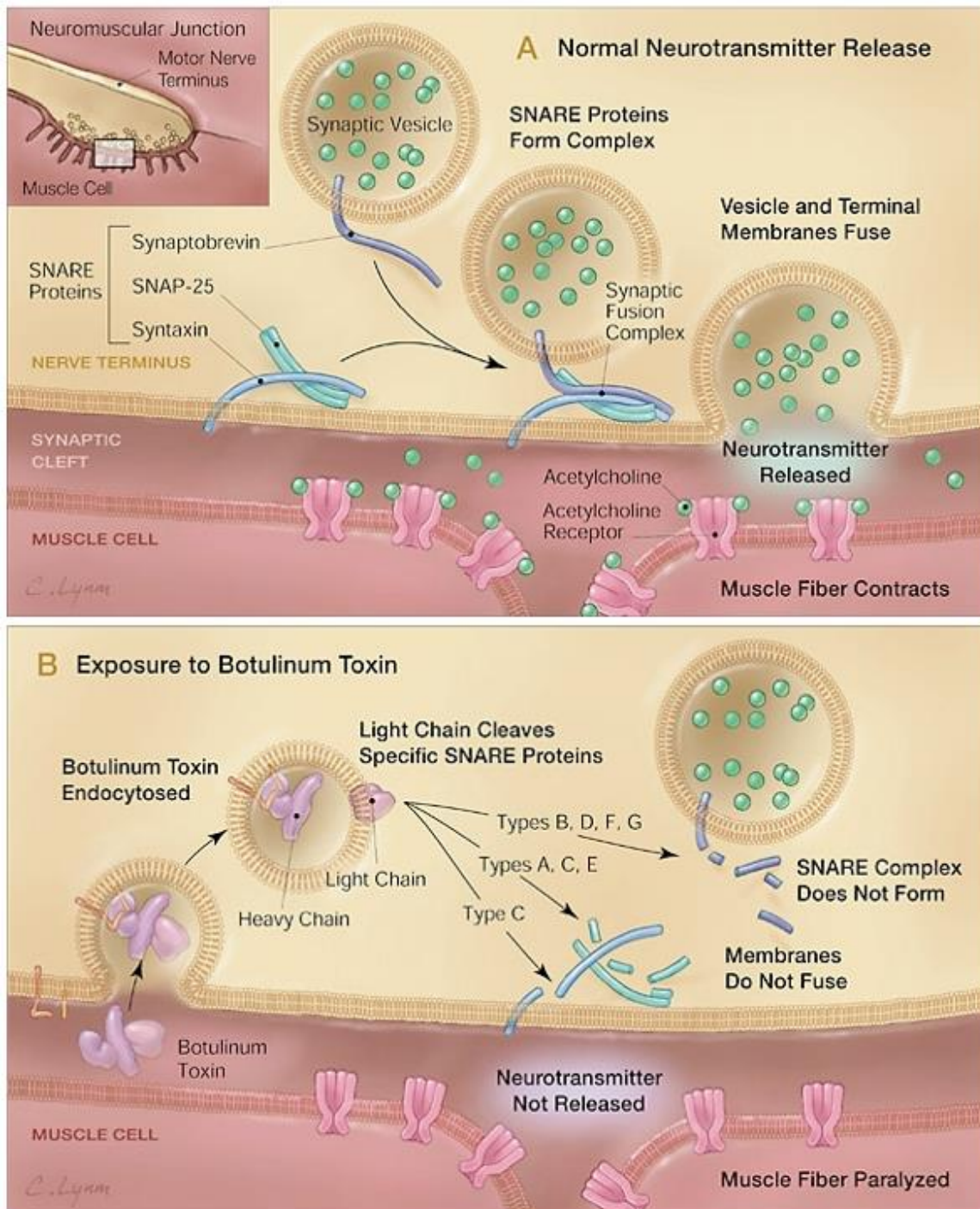


Figure 20: Mechanism of Action of Botulinum toxin

Botulinum toxin used in this study is a sterile, lyophilized purified form of botulinum toxin type A, produced from a culture of the Hall strain of *Clostridium botulinum* grown in medium containing N-Z amine and yeast extract. Each vial contains 100 IU of BTX- A, 0.5 mg of albumin and 0.9 mg of sodium chloride. It is reconstituted with normal saline. The reconstituted solution is to be used within 24 hours, care is taken to avoid shaking of the vial, and storage is done in the refrigerator at a temperature of 2-8 °C.²⁹ There is no clinical standardization on the use of Botulinum toxin. Factors which affect clinical response are dosage, commercial preparation, storage, immunogenicity, reconstitution and most importantly anatomy of the particular region of injection.^{30, 31}

4000 IU is considered as lethal dose. Maximum advised dosage is 200 IU. However, a dosage of 10-50 IU is advised in treatment of chronic fissure in ano. The dosage is not found to be related to therapeutic efficacy.³² Bobkiewicz et al studied the effect of a range of dosages in 1577 patients receiving Botulinum toxin ranging from as less as 5 to as high as 150 units. There was a similar profile of efficacy in all the patients.



Figure 21: Vial of Botulinum toxin commercially available

Apart from cholinergic endings at the neuromuscular junction, Botulinum toxin can affect the autonomic pre- and post-ganglionic synapses and the synapse-rich areas of the hippocampus and cerebellum, as well as Renshaw cells. When introduced into noncholinergic nerve terminals, release of many neurotransmitters can be blocked. It is also more effective in blocking neuromuscular junctions when the target muscle is active, thus producing an autofocusing effect. These autonomic and non-cholinergic effects formed the rationale for its clinical application in fissure in ano.

Presynaptic parasympathetic terminal blockade in internal sphincter, should cause inhibition of parasympathetic mediated relaxation of the internal sphincter, however following mechanism actually helps in relaxation of the internal sphincter:

- Action a preganglionic terminal, prevents release of adrenaline also. Adrenaline causes tonic sympathetic contraction, which is the dominant action.
- There is an unopposed action of the non A non C transmitter due to inhibition at presynaptic terminal. Release of nitric oxide causes relaxation of the sphincter.

The therapeutic effect of Botulinum toxin takes an average of 3 hours to occur, and last for 5-6 weeks on an average when there is sprouting of new neuromuscular junctions. Adverse effects of the toxin have been widely studied, and it is generally considered a safe drug when used in moderate dosage. Local muscle weakness represents the expected pharmacological action. Local effects may occur such as pain, bruising, inflammation, hypoesthesia.^{33,34}

A systematic review and meta-analysis conducted by Shao et al in 2009, compared 4 different randomised controlled trials which compared effectiveness of botulinum toxin injection. They collected data from 279 patients involved in the 4 trials.

It was found that lateral internal sphincterotomy was more effective in the treatment of fissure in ano.³⁵

MATERIALS AND METHODOLOGY

Study Centre

Madras Medical College and Rajiv Gandhi Government General Hospital, Chennai

Duration of Study

January 2018 to September 2019

Study Design

Randomized Control Trial with Single Blinding

Sample Size

60

Inclusion Criteria

All patients with a chronic fissure in ano

Exclusion Criteria

- Any patient with an acute fissure in ano.
- Patients with additional hemorrhoids, fistulae in ano, inflammatory bowel disease
- Patients with allergic reaction to botulinum toxin
- Patients with co-morbid- diabetes, hypertension, seizure or thyroid disorder, or any drugs which may alter treatment
- Patients undergoing any other treatment modality for the same disease

Ethics Clearance

Approved

Methodology

A detailed questionnaire (Annexure 5) was filled in prospectively, noting all the clinical, radiological and biochemical parameters of each of the participants of the study.

Informed written consent (Annexure 4) was obtained in the patients own language, after reading out the patient information sheet (Annexure 3).

60 consecutive patients, who

- consent to participate in the study and,
- fit the inclusion criteria

were randomly divided into two study groups using SNOSE or sequentially numbered, opaque sealed envelopes. Each participant picked up an envelope deciding the treatment they would receive: one half receiving the gold standard treatment- lateral internal sphincterotomy and the other receiving botulinum toxin injection.

Lateral Internal Sphincterotomy was done under spinal anesthesia or IV sedation as seen fit by the anesthetist. With the patient in lithotomy position, parts painted and draped; an incision was made at 3 or 9 o'clock position at anal verge.



Figure 22: Anal fissure in a patient

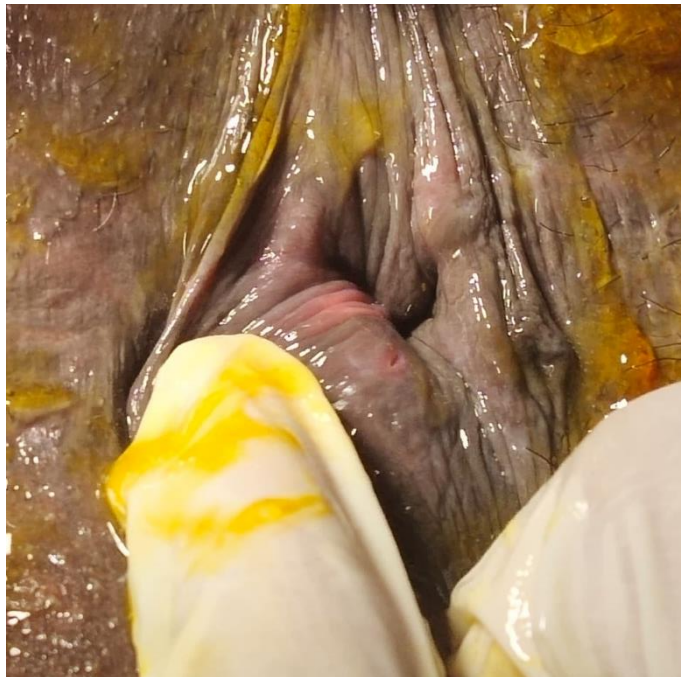


Figure 23: Anal fissure in another patient



Figure 24: Dissection of internal sphincter fibres

The fibres from the free edge of the internal sphincter are dissected out using forceps and divided. Wound left open to granulate. Sterile pack applied.



Figure 25: Cutting of the fibres

Botulinum Toxin was reconstituted with normal saline to create strength of 20 IU/ml. Using an insulin syringe and 26 gauge needle, 0.5 ml of solution was injected on either sides of the fissure at 4 o'clock and 8 o'clock position.



Figure 26: Reconstituted toxin with insulin syringe

The entire technique was done in lithotomy position, under mild IV sedation. The dosage of toxin injected was standardized in this study to 20 IU. The injection was done into the internal sphincter by entering the intersphincteric groove.

However, many studies have demonstrated that the site of injection was not very important due to drug diffusion of 1-2 cm. Hence injection into internal sphincter or the intersphincteric groove had a comparable result in the relaxation of internal sphincter.



Figure 27: Injection of botulinum toxin in a female patient



Figure 28: Injection of botulinum toxin in a male patient

All the patients received an induction antibiotic at the start of procedure. Sitz bath was advised post operatively for 1 week four times a day in warm water. Post operative analgesia was given for two days using T.Paracetamol 500mg TDS, and prolonged if needed.

Patients were followed for 3 months postoperatively and evaluated in terms of post operative pain relief, post operative complications, healing of fissure and recurrence rates. The outcomes measured in this study are as below:

- The primary outcome measure were relief of pain and healing of the anal fissure.
- Secondary end points include complications such as wound infection, incontinence and rate of recurrence

The collected data were analysed with IBM - SPSS statistics software 23.0 Version.

Definitions used in the Study:

Relief of pain defined as complete absence of pain. Pain was quantified by the numerical rating scale 0-10; 0 being no pain and 10 being worst pain imaginable.

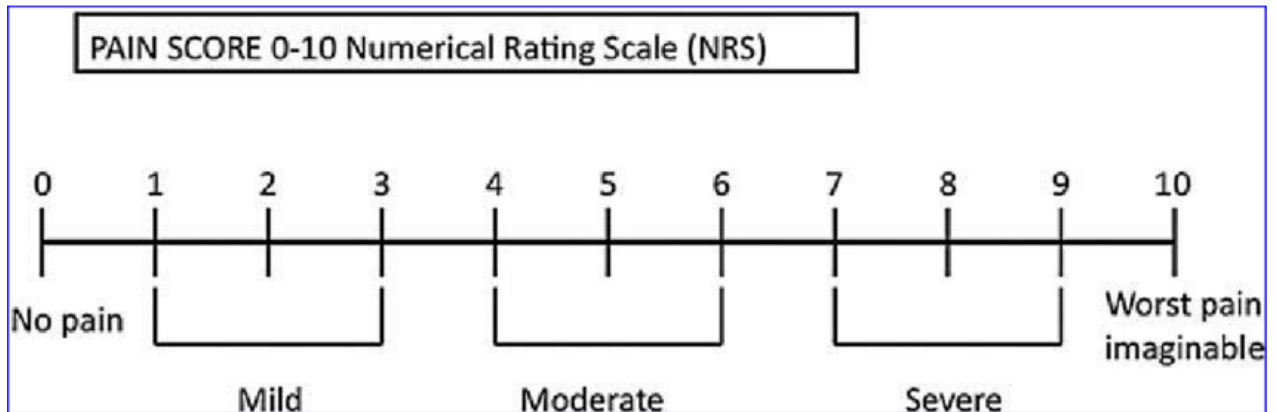


Figure 29: Numerical Pain Scale

Return to daily activities indicates complete capacity to do activities as done by the patient previously, including and not restricted to eating, dressing, getting into or out of a bed or chair, taking a bath and using the toilet, going to work.

Healing of fissure was the primary end point of the study, and defined as complete resolving of the fissure with the formation of a scar. This was measured at 6 weeks post surgery and confirmed at 3 months post surgery.

Post operative complications were also studied. Wound infection was defined as presence of erythema, edema, induration or discharge. These were noted at 1 day post operatively and 1 week post operatively.

Incontinence was monitored by asking the patient to maintain a diary for the entire duration of follow up and note any soiling, passing of feces or flatus without awareness. This was calculated by using the Jorge-Wexner score at both 6 weeks and 3 months post operatively.

Table 1: Jorge-Wexner Score

<i>Type of incontinence</i>	<i>Frequency</i>				
	<i>Never</i>	<i>Rarely</i>	<i>Sometimes</i>	<i>Usually</i>	<i>Always</i>
Solid	0	1	2	3	4
Liquid	0	1	2	3	4
Gas	0	1	2	3	4
Wears pad	0	1	2	3	4
Lifestyle alteration	0	1	2	3	4

Never, 0; rarely, <1/month; sometimes, <1/week, ≥1/month; usually, <1/day, ≥1/week; always, ≥1/day.

0, perfect; 20, complete incontinence.

The frequency of incontinence to

- solid,
- liquid,
- gas,
- wearing of pad,
- lifestyle alteration

was notes and score calculated.

Frequency was categorised as

- Never: no occurrence
- Rarely: less than 1 incidence in a month

- Sometimes: more than once a month, but less than once a week
- Usually: more than once a week, but less than once a day
- Always: more than once a day

The highest possible score of 20 indicated complete incontinence. On the other hand a score of 0 implied a continent sphincter.

Recurrence was defined as the occurrence of fissure in ano at the same site, post treatment by either modality, after initial resolving of the fissure.

RESULTS

- The collected data were analyzed with IBM.SPSS statistics software 23.0 Version.
- To describe about the data descriptive statistics frequency analysis, percentage analysis were used for categorical variables and the mean & standard deviation were used for continuous variables.
- To find the significant difference between the bivariate samples in Independent groups the Unpaired sample t-test was used.
- To find the significance in categorical data Chi-Square test was used similarly if the expected cell frequency is less than 5 in 2×2 tables then the Fisher's Exact was used.
- In all the above statistical tools the probability value .05 is considered as significant level.

Demographic Data

Age of the patients who participated in the study was.

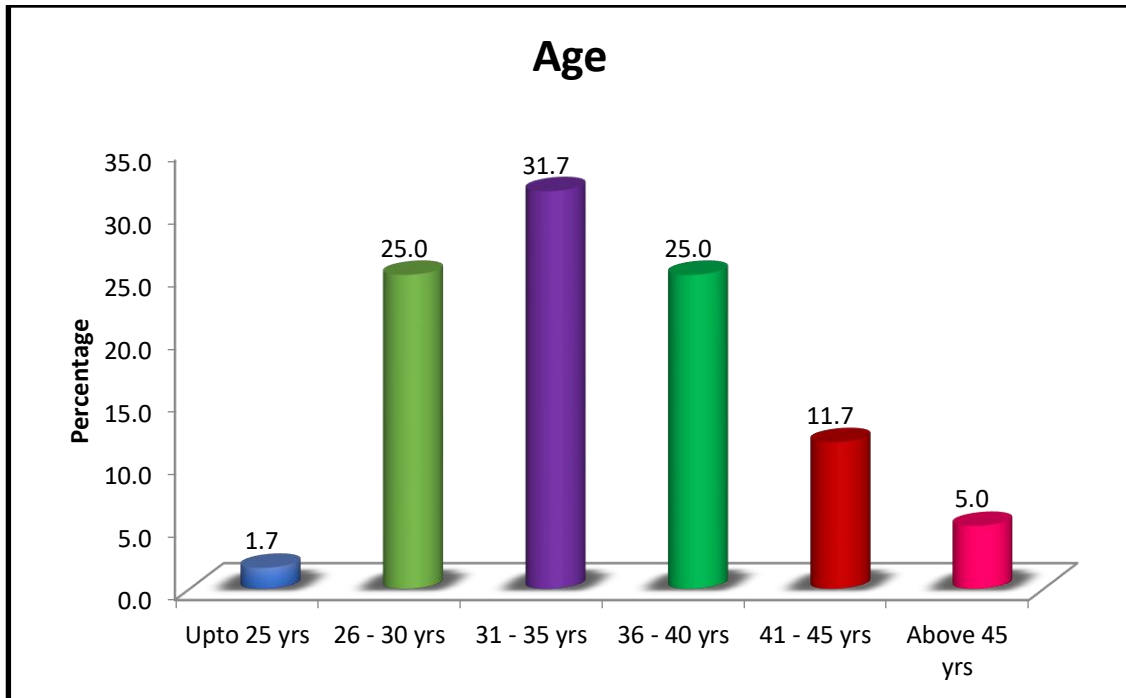


Figure 30: Age Distribution

Table 2: Age Distribution

Age of the patients in the study		
	Frequency	Percent
Upto 25 yrs	1	1.7
26 - 30 yrs	15	25.0
31 - 35 yrs	19	31.7
36 - 40 yrs	15	25.0
41 - 45 yrs	7	11.7
Above 45 yrs	3	5.0
Total	60	100.0

The patients were randomly divided into groups of 30 each. The mean age of the case group was 35.27, with a standard deviation of 5.9; and the mean age of the control group was 34.20, with a standard deviation of 5.3

Table 3: Comparison of age

Comparison of Age between Groups				
Age	Groups		Total	P-value
	Cases	Controls		
Upto 25 yrs	0	1	1	0.648
26 - 30 yrs	8	7	15	
31 - 35 yrs	9	10	19	
36 - 40 yrs	6	9	15	
41 - 45 yrs	5	2	7	
Above 45 yrs	2	1	3	
Total	30	30	60	

P value of the age weighted comparison between the cases and control was .65, and hence not significant. Thus, the two groups are comparable age- wise.

Of the 60 participants, 35 were male and 25 female.

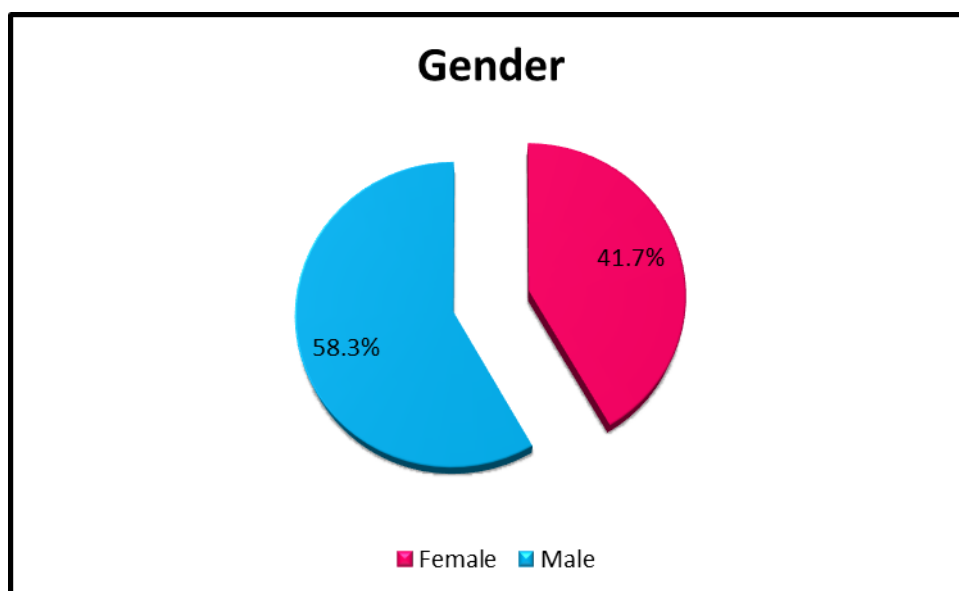


Figure 31: Gender distribution

The cases were 19 males and 11 females, whereas controls had 16 males and 14 females.

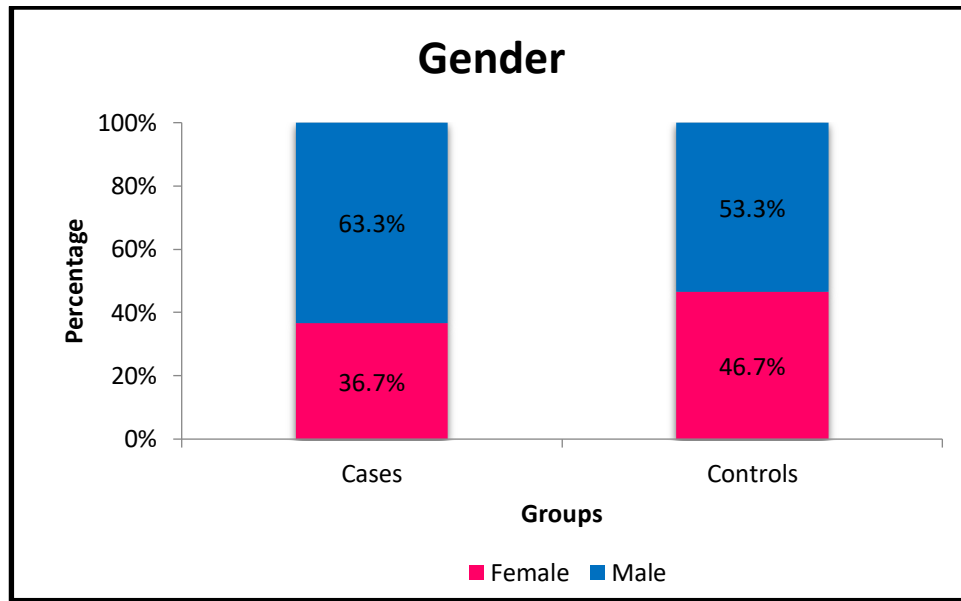


Figure 32: Gender distribution between groups

Using, t- test, the gender distribution between the two groups was found to have a value of 0.432, which is more than 0.05, and hence, not significant.

Table 4: Comparison of Gender

Comparison of Gender between groups						
			Groups		Total	P-value
			Cases	Controls		
Sex	Female	Count	11	14	25	0.432
		%	36.7%	46.7%	41.7%	
	Male	Count	19	16	35	
		%	63.3%	53.3%	58.3%	
Total	Count	30	30	60		
	%	100.0%	100.0%	100.0%		

Clinical Data

Relief of pain was measured using the Numerical pain scale after 1 day and 1 week post operatively. If the participant denoted a value of zero, it was categorised as 'NO' pain. Any value above 1, was categorised as having pain.

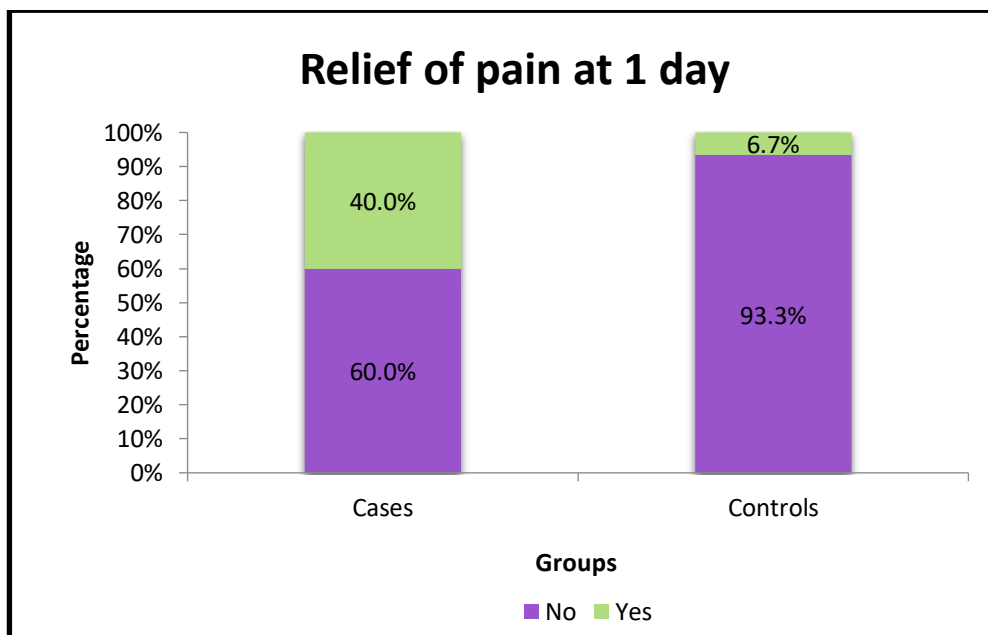


Figure 33: Comparison of relief of pain at 1 day

There was a massive difference in relief of pain in the cases when compared to the control group.

12 participants, of 30, about 40% had complete relief of pain after Botulinum toxin injection. On the other hand, only 6.7% of the control group, 2 participants had complete relief of pain at 1st post operative day.

Table 5: Comparison of Pain relief at 1 day

Comparison of Relief of pain at 1 day between Groups							
			Groups		Total	χ^2 - value	P-value
			Cases	Controls			
Relief of pain at 1 day	No	Count	18	28	46	9.317	0.002 **
		%	60.0%	93.3%	76.7%		
	Yes	Count	12	2	14		
		%	40.0%	6.7%	23.3%		
Total	Count	30	30	60			
	%	100.0%	100.0%	100.0%			

** Highly Significant at P < 0.01 level

As can be seen from the frequencies cross tabulated above, there is a significant relief of pain with $\chi^2 = (1, N=60) = 9.3, p = 0.002$.

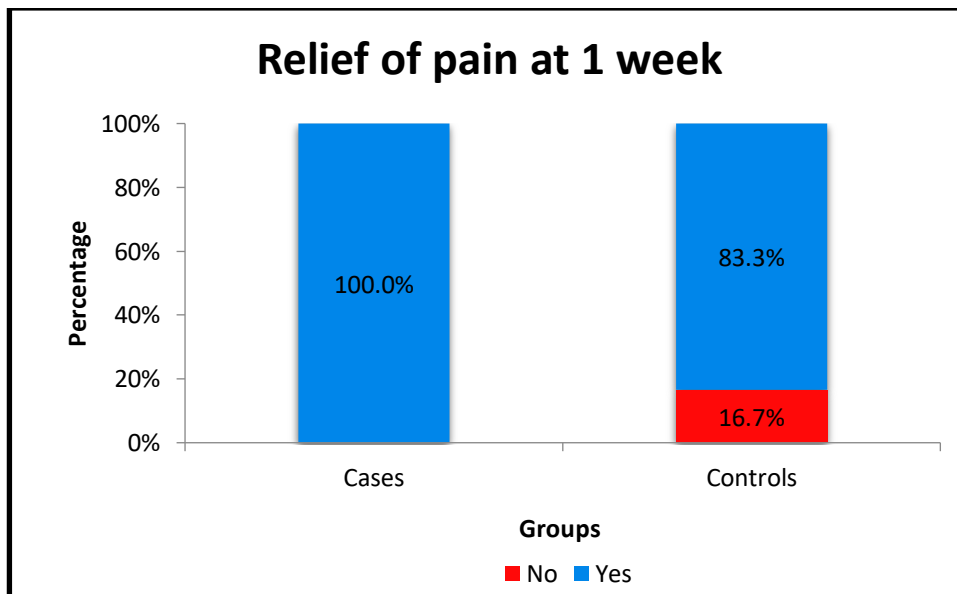


Figure 34: Comparison of relief of pain at 1 week

Relief of pain after 1 week was present in all 30 participants in the patients who received Botulinum toxin injection, whereas in patients who underwent lateral internal sphincterotomy it was present in 25 members. The difference between the two groups was significant $\chi^2(1, N=60) = 5.45, p=.02$.

Table 6: Comparison of pain relief at 1 week

Comparison of Relief of pain at 1 week between Groups							
			Groups		Total	χ^2 - value	P-value
			Cases	Controls			
Relief of Pain at 1 week	No	Count	0	5	5	5.455	0.020 *
		%	0.0%	16.7%	8.3%		
	Yes	Count	30	25	55		
		%	100.0%	83.3%	91.7%		
Total	Count	30	30	60			
	%	100.0%	100.0%	100.0%			

* Significant at P < 0.05 level

The next variable studied was the number of days to **return to daily activities**.

Table 7: Comparison of return to daily activities

Comparison of Return to daily activity <3 days between Groups							
			Groups		Total	χ^2 value	P-value
			Cases	Controls			
Return to daily activity <3 days	No	Count	8	23	31	15.017	0.0005**
		%	26.7%	76.7%	51.7%		
	Yes	Count	22	7	29		
		%	73.3%	23.3%	48.3%		
Total	Count	30	30	60			
	%	100.0%	100.0%	100.0%			

** Highly Significant at P < 0.01 level

Among the cases, 22 members returned to daily activities before POD 3, whereas only 7 members in the control group had done the same. This difference between the two groups was highly significant $\chi^2(1, N=60) = 15.01, p < .001$.

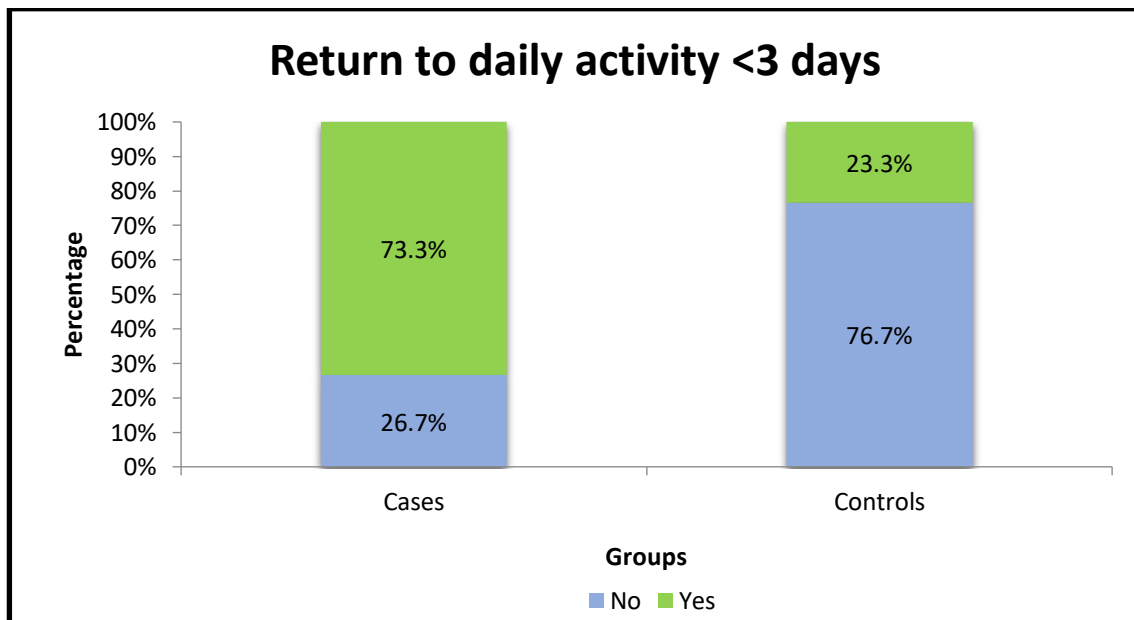


Figure 35: Comparison of return to daily activity

Among the cases, the mean number of days to return to daily activities was 2 with a SD of 0.59. Among the controls, mean number of days to return to daily activities was 4 with a SD of 1.65.

Table 8: Comparison of Return to daily activities

Comparison of Return to daily activities at POD by Independent sample t-test						
Groups		N	Mean	S.D	t-value	P-value
Return to daily activities at POD	Cases	30	2	0.59	4.694	0.0005 **
	Controls	30	4	1.65		
** Highly Significant at P < 0.01 level						

Using independent samples t-test, this was found to be highly significant, $t = -4.694$, $p = .0005$.

Healing of fissure was more in the patients who underwent surgery, with 90% healing at 6 weeks post operatively compared to 76.7% healing in patients receiving Botulinum toxin

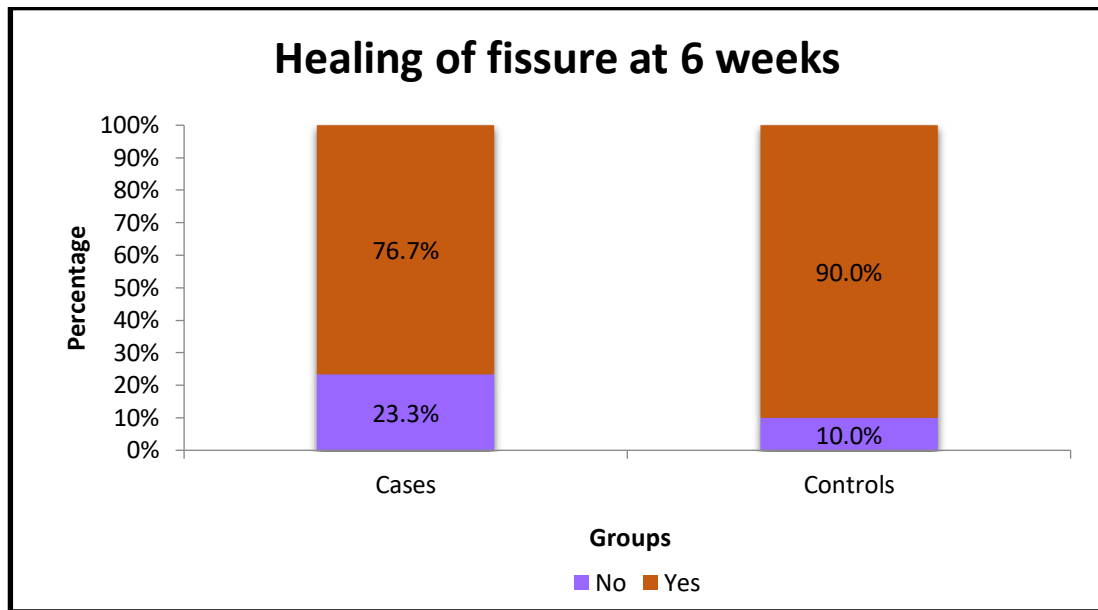


Figure 36: Comparison of healing at 6 weeks

However, the difference in the healing between the cases and controls was not found to be significant. $\chi^2(1, N=60) = 1.92, p = .16$

Table 9: Comparison of healing at 6 weeks

Comparison of Healing of fissure at 6 weeks between Groups							
			Groups		Total	χ^2 value	P-value
			Cases	Controls			
Healing of fissure at 6 weeks	No	Count	7	3	10	1.920	0.166 #
		%	23.3%	10.0%	16.7%		
	Yes	Count	23	27	50		
		%	76.7%	90.0%	83.3%		
Total	Count	30	30	60			
	%	100.0%	100.0%	100.0%			

No Significant at P < 0.05 level

Healing of the anal fissure at 3 months was present in 59 patients studied, with just one patient in the case group, who had a small residual fissure at the same site with partial scarring. However, the patient was asymptomatic.

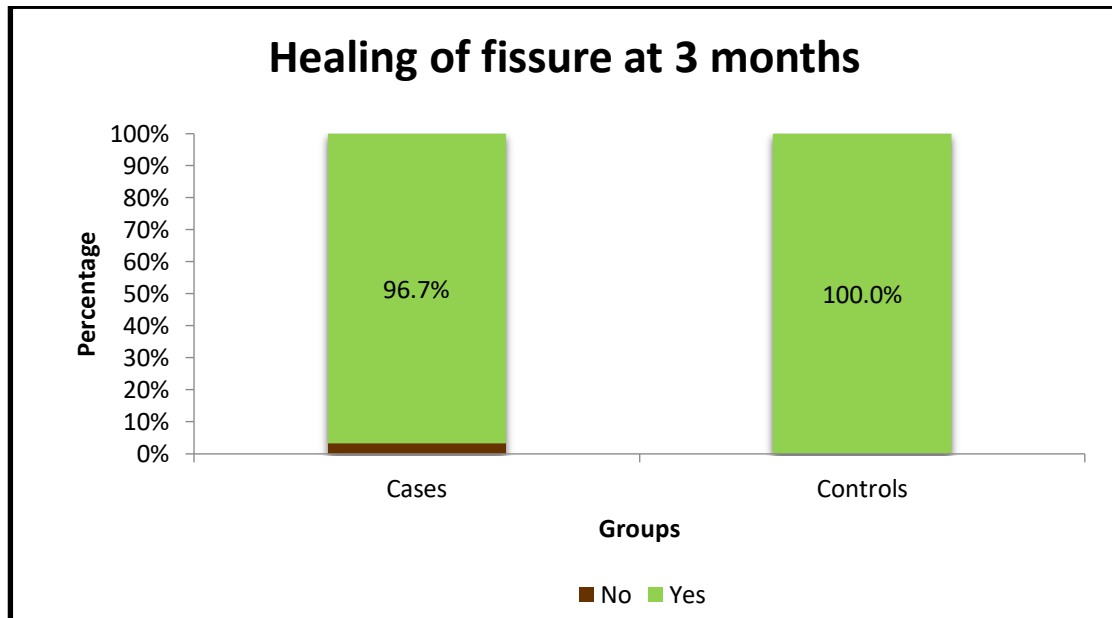


Figure 37: Comparison of healing at 3 months

The difference in the healing rates between the two methods was not found to be statistically significant, $p=.313$, using Fisher's exact test

Table 10: Comparison of healing at 3 months

Comparison of Healing of fissure at 3 months between Groups						
			Groups		Total	P-value
			Cases	Controls		
Healing of fissure at 3 months	No	Count	1	0	1	0.313 #
		%	3.3%	0.0%	1.7%	
	Yes	Count	29	30	59	
		%	96.7%	100.0%	98.3%	
Total	Count	30	30	60		
	%	100.0%	100.0%	100.0%		

No Significant at $P < 0.05$ level

Wound infection was present in two patients who underwent lateral internal sphincterotomy, but none of the patients who had Botulinum toxin injection. The following figure represents it clearly.

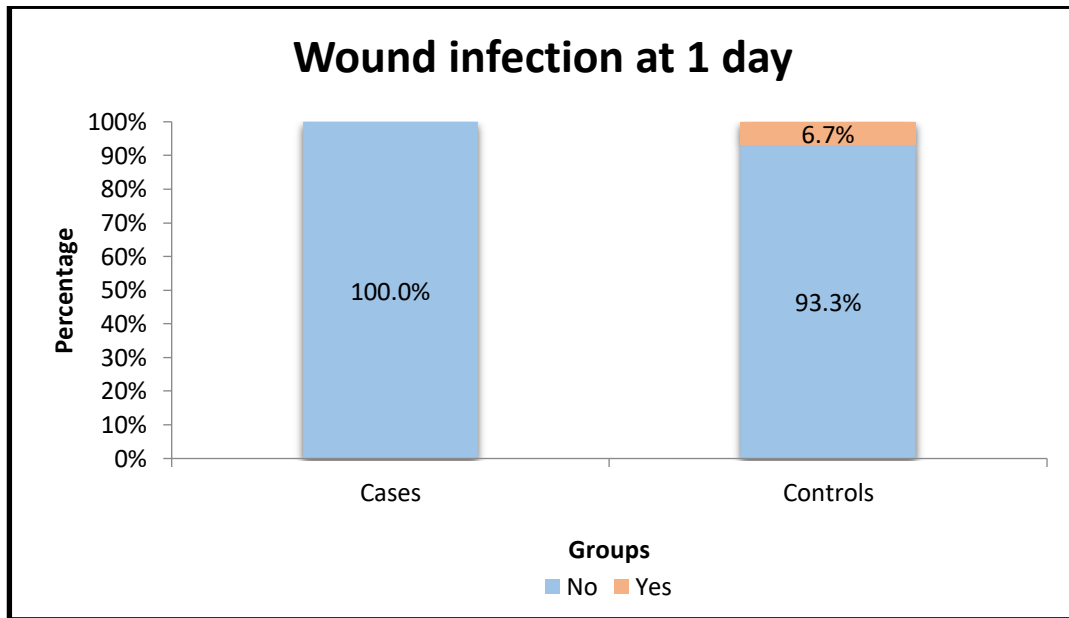


Figure 38: Comparison of wound infection at 1 day

On comparing between the two groups, the incidence of wound infection was found to be insignificant 0 versus 6.7%, $p=.15$ (Fishers’s exact test)

Table 11: Comparison of wound infection at 1 day

Comparison of Wound infection at 1 day between Groups						
			Groups		Total	P-value
			Cases	Controls		
Wound infection at 1 day	No	Count	30	28	58	0.150 #
		%	100.0%	93.3%	96.7%	
	Yes	Count	0	2	2	
		%	0.0%	6.7%	3.3%	
Total	Count	30	30	60		
	%	100.0%	100.0%	100.0%		

No Significant at $P < 0.05$ level

After 1 week of procedure, only 1 of the 2 patients still had wound infection in the control group with minimal purulent discharge. This patient was treated with appropriate antibiotics and resolution occurred in a few days. Yet another patient developed edema of wound at the 1 week follow up.

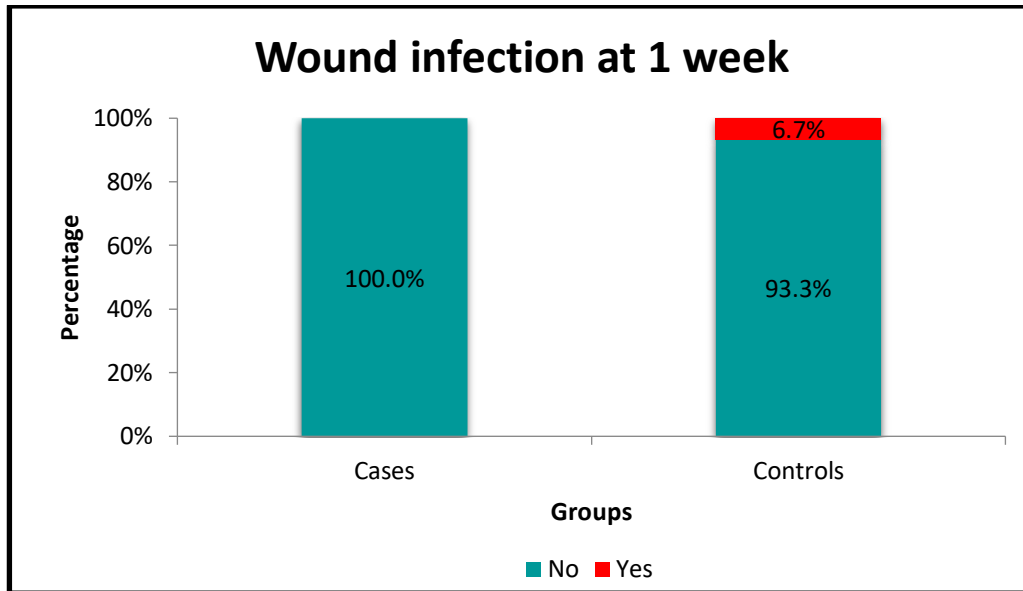


Figure 39: Comparison of wound infection at 1 week

Using Fisher’s exact test, p value was .15, and there was no significant difference between the case and control groups regarding wound infection.

Table 12: Comparison of wound infection at 1 week

Comparison of Wound infection at 1 week between Groups						
			Groups		Total	P-value
			Cases	Controls		
Wound infection at 1 week	No	Count	30	28	58	0.150 #
		%	100.0%	93.3%	96.7%	
	Yes	Count	0	2	2	
		%	0.0%	6.7%	3.3%	
Total	Count	30	30	60		
	%	100.0%	100.0%	100.0%		

No Significant at P < 0.05 level

Incontinence of sphincter was determined in the patients by asking detailed loss of control over passing flatus, liquid or solid stools, as well as the need to use a pad, or significant lifestyle changes with regards to anal sphincter tone.

At end of 6 week follow up period, 2 participants or 6.7% who underwent Botulinum toxin had incontinence, whereas 8 participants or 26.7% in the sphincterotomy group had incontinence.

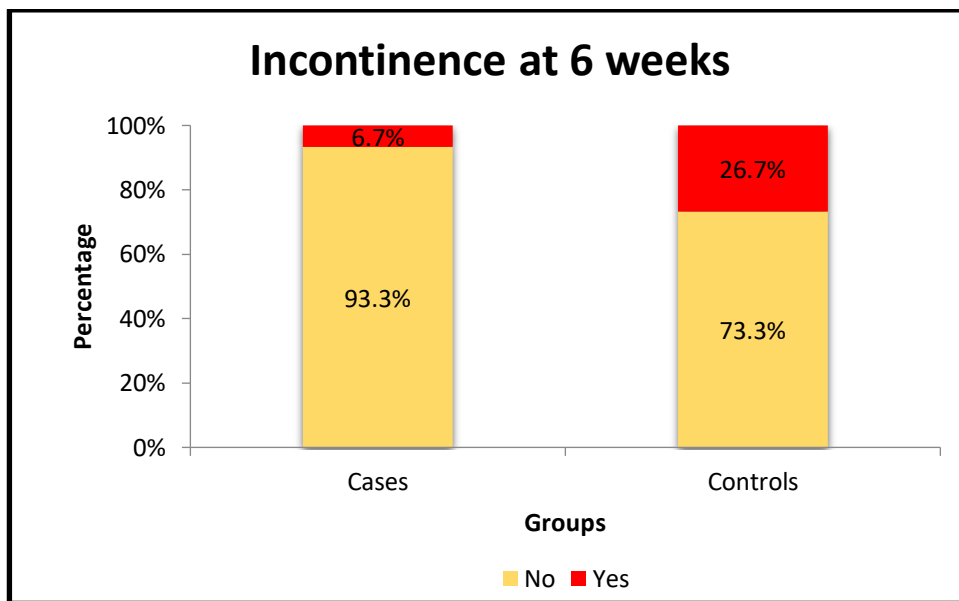


Figure 40: Comparison of incontinence at 6 weeks

Of the people who had incontinence in the case group, the Wexner scores were 4 and 2. The Wexner scores were 7, 4, 4, 6, 3, 4, 3, and 6 in the control group.

Table 13: Comparison of Incontinence at 6 weeks

Comparison of Incontinence at 6 weeks between Groups							
			Groups		Total	χ^2 value	P-value
			Cases	Controls			
Incontinence at 6 weeks	No	Count	28	22	50	4.32	0.80 #
		%	93.3%	73.3%	83.3%		
	Yes	Count	2	8	10		
		%	6.7%	26.7%	16.7%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		

No Significant at P < 0.05 level

However statistically, the difference between the two groups regarding incontinence at 6 weeks post procedure was not significant, $\chi^2(1, N=60) = 4.32, p=.8$

3 months after the procedure, there was an improvement in symptoms for the patients who experienced incontinence.

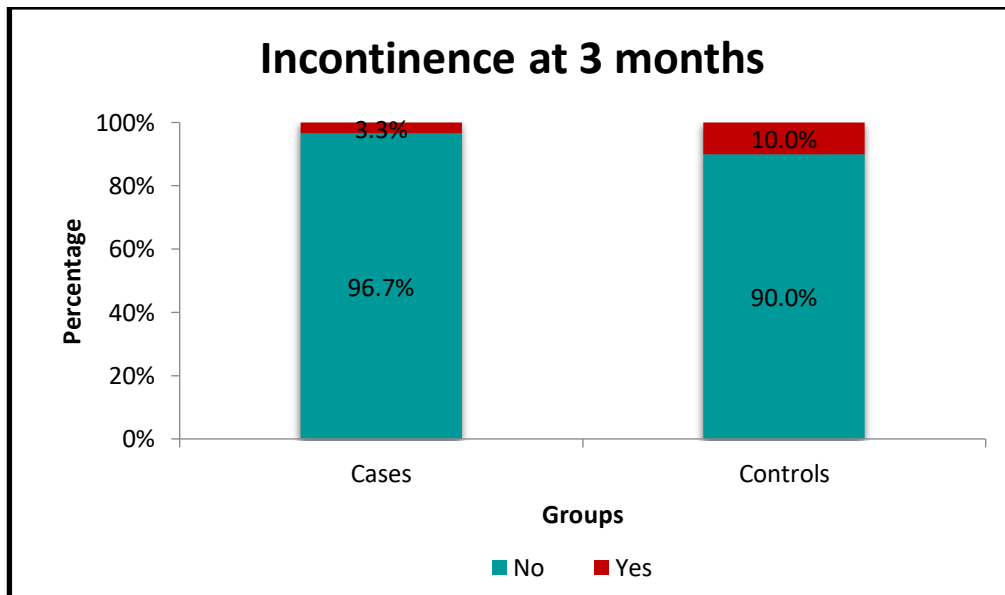


Figure 41: Comparison of incontinence at 3 months

Only one patient (3.3%) in the case group complained of incontinence to flatus, with a Wexner score of 3.

3 patients (10%) in the control group still complained of incontinence, with Wexner scores of 3, 3 and 2.

Table 14: Comparison of Incontinence at 3 months

Comparison of Incontinence at 3 months between Groups							
			Groups		Total	χ ² - value	P-value
			Cases	Controls			
Incontinence at 3 months	No	Count	29	27	56	0.301	0.612 #
		%	96.7%	90.0%	93.3%		
	Yes	Count	1	3	4		
		%	3.3%	10.0%	6.7%		
Total		Count	30	30	60		
		%	100.0%	100.0%	100.0%		
# No Significant at P < 0.05 level							

As seen in the above tabulated data, there is no significant difference in incontinence at 3 months between sphincterotomy and Botulinum toxin injection.

However on comparing the two groups, incontinence is four times higher in the patients who underwent sphincterotomy at 6 weeks.

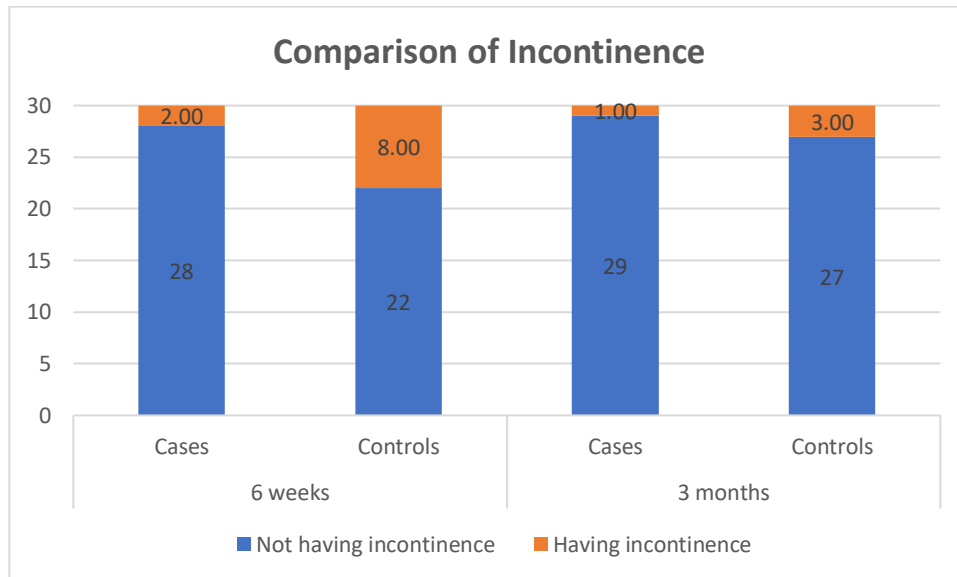


Figure 42: Number of patients having incontinence

The Wexner scores at 6 weeks, were significantly lower in the patients who had Botulinum toxin injection. However, at 3 months, the difference in the scores was no longer valid.

Recurrence of anal fissure after treatment by either method was present in 2 of the 60 patients: one each in test and control group, bringing the incidence of recurrence post procedure to 3%. This was present after documentation of scar formation at 6 weeks.

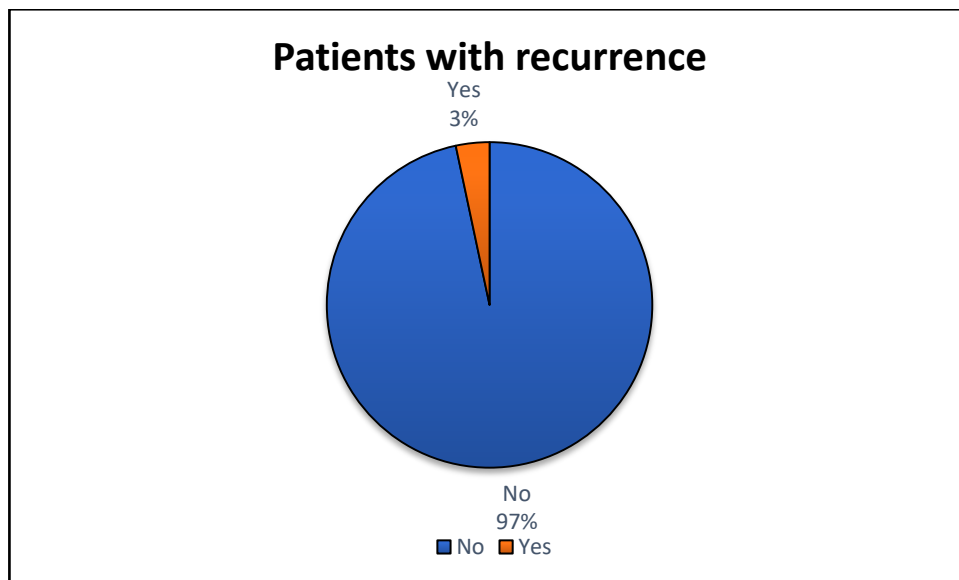


Figure 43: Total recurrence

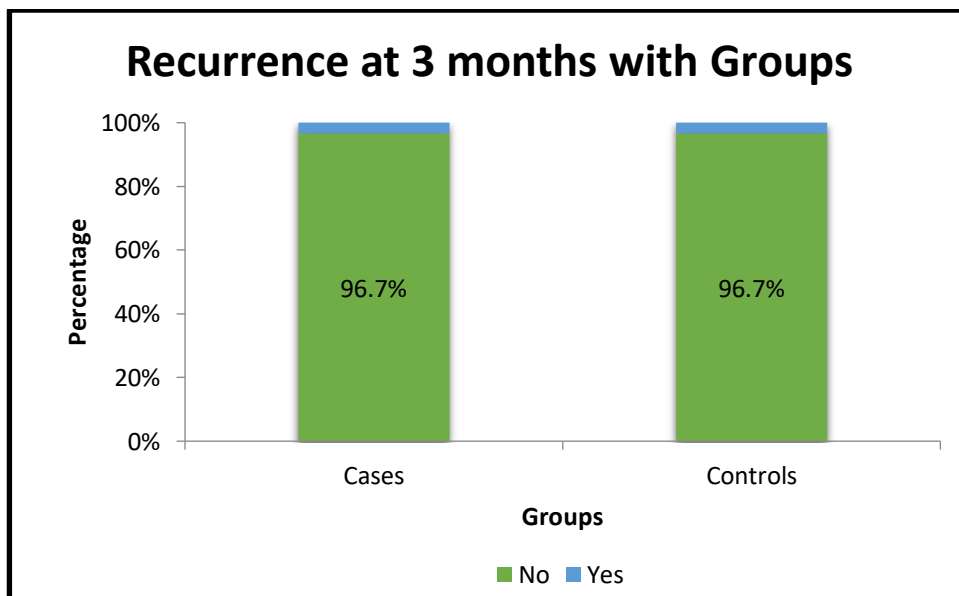


Figure 44: Recurrence at 3 months

Both the groups had one recurrence and hence, there was no difference between the two, p=1.

Table 15: Comparison of recurrence at 3 months

Comparison of Recurrence at 3 months between Groups							
			Groups		Total	χ ² - value	P-value
			Cases	Controls			
Recurrence at 3 months	No	Count	29	29	58	0.000	1.000 #
		%	96.7%	96.7%	96.7%		
	Yes	Count	1	1	2		
		%	3.3%	3.3%	3.3%		
Total	Count	30	30	60			
	%	100.0%	100.0%	100.0%			

No Significant at P < 0.05 level

DISCUSSION

All the patients in the study group were aged between 24 and 48 years of age. The groups were equally age and sex- weighted unintentionally when the statistics were run. These helps the study to alleviate any bias due to age or gender of the patient.

The single biggest complaint of patients suffering from chronic anal fissure is the sharp pain, which alters life and brings about a fear of defecation. In this study, post procedure relief of pain was significantly different between patients undergoing lateral internal sphincterotomy and botulinum toxin injection. This shows that botulinum toxin injection provides faster relief from symptoms. It also helps in combating post operative pain at the site.

After 1 week of surgery, patients having sphincterotomy also reported improvement in pain. However it was not present in all patients like in the botulinum toxin receivers. Lower rates of pain relief in sphincterotomy group can be a reason for attempting alternate methods.

Probably the most important factor for a patient is early return to normalcy after an interventional procedure. There was a notable difference between the two methods in this aspect, with the surgery group reporting delay in returning to routine by an average of 2 days. Ability to perform activities of daily life independently and resume work at the earliest are an added advantage while using Botulinum toxin injection.

Healing of fissure between both the groups was not statistically different. At 6 weeks post operatively, there were marginally more members in the sphincterotomy group with healed fissures. After 3 months of follow up, there was healing of fissure in both the groups.

This shows that both the treatment methods are similar in their primary use- healing of fissure. This is probably since both involve the same mechanism of action which is weakening of the internal sphincter, so as to provide improved perfusion, thus healing the fissure.

Wound infection is a complication of most surgeries. In this study, the anatomy of the region as well as close proximity of wound and daily contact with stools increased the chances of wound infection. Early post operative infection was detected in the sphincterotomy cases. It was probably due to the small stab wound which was left open.

These patients alone received antibiotics, resulting in partial resolution. However, there was no significant difference between the two groups and hence they are comparable in this aspect.

Post operative the maximum complaint the sphincterotomy group was the incontinence to flatus and sometimes to liquid stools. Early post operative incontinence was four times higher in the sphincterotomy group. While this was not statistically significant, the percentage of patients developing incontinence after a widely used surgery is alarming- almost 26% in this study.

With time, the anal tone was found to improve, and the incontinence rates at 3 months after surgery were at 10% in the patients who underwent lateral internal sphincterotomy. Patients receiving Botulinum toxin also had complaints of incontinence. However this was much lower. 6.7% at 6 weeks after procedure and 3.3% after 3 months post procedure.

Botulinum toxin injection is probably safer in terms of incontinence in terms of absolute numbers. Wexner score used to assess the incontinence levels was instrumental in detecting the difference between the two groups. Among the patients describing incontinence, the Wexner score was statistically higher in the patients undergoing sphincterotomy at 6 weeks, but not at 3 months.

Recurrence was checked for at 3 months after surgery. Any patient who started to have healing of fissure during the follow up period and then presented with a fissure at same or new site was categorised as treatment failure. In this study, a patient from each group presented with recurrence. So, there was no difference between the treatment modalities. However, both the patients were completely asymptomatic, and fissure was discovered at the time of examination. The patients were informed about the recurrence and long term follow up and further treatment advised in case of any symptoms.

Scope of improvement

This study could have been further benefited by involving a higher sample size. The follow up period was adequate to study the research questions at hand. However long term progression of the disease post treatment would have been interesting to compare.

CONCLUSION

The study indicates that botulinum toxin and lateral internal sphincterotomy are equally effective in terms of disease cure rates.

The post operative complications are lower with the use of Botulinum toxin- both in terms of pain and incontinence. Return to daily activities was also established to be superior with Botulinum toxin injection compared to lateral internal sphincterotomy. There is no difference in the incidence of wound infection.

Recurrence rates comparable in the two groups.

Hence, Botulinum toxin may be used as an effective alternative to lateral internal sphincterotomy with improved adverse effect profile and early resolving of disease at hand. It is also an easier technique which can be done as an office procedure. Need for anesthesia during procedure and analgesia postoperatively were reduced, thereby increasing the attractiveness of this modality.

REFERENCES

1. Yeo CJ. Shackelford's Surgery of the Alimentary Tract, E-Book. Elsevier Health Sciences; 2017 Dec 18.
2. SHAFIK A, DOSS S. Surgical anatomy of the somatic terminal innervation to the anal and urethral sphincters: role in anal and urethral surgery. *The Journal of urology*. 1999 Jan;161(1):85-9.
3. Bansal N, Sachdeva M, Jain P, Ranjan P, Arora A. Anorectal manometry: current techniques and indications. *JIMSA*. 2013 Jul;26(3):169-70.
4. Baijal R, Jain M. Analysis of Indications and Results of Anorectal Manometry in Two Tertiary Hospitals in India. *Arch Clin Gastroenterol*. 2017;3(1):009-10.
5. Jonas M, Scholefield JH. Anal Fissure. *Gastroenterol Clin North Am*. 2001;30:167–181.
6. Oh C, Divino CM, Steinhagen RM. Anal fissure: 20-year experience. *Dis Colon Rectum*. 1995;38:378–382.
7. Lund JN, Scholefield JH. Aetiology and treatment of anal fissure. *British journal of surgery*. 1996 Oct 1;83(10):1335-44.
8. Klosterhalfen B, Vogel P, Rixen H, Mittermayer C. Topography of the inferior rectal artery: a possible cause of chronic, primary anal fissure. *Diseases of the Colon & Rectum*. 1989 Jan 1;32(1):43-52.
9. Schouten WR, Briel JW, Auwerda JJ, De Graaf EJ. Ischaemic nature of anal fissure. *British journal of surgery*. 1996 Jan;83(1):63-5.
10. Schouten WR, Briel JW, Auwerda JJ. Relationship between anal pressure and anodermal blood flow. *Diseases of the colon & rectum*. 1994 Jul 1;37(7):664-9.

11. Gupta PJ. Randomized, controlled study comparing sitz-bath and no-sitz-bath treatments in patients with acute anal fissures. *ANZ journal of surgery*. 2006 Aug;76(8):718-21.
12. Oettle GJ. Glyceryl trinitrate vs. sphincterotomy for treatment of chronic fissure-in-ano. *Diseases of the colon & rectum*. 1997 Nov 1;40(11):1318-20.
13. Richard CS, Gregoire R, Plewes EA, Silverman R, Burul C, Buie D, Reznick R, Ross T, Burnstein M, O'Connor BI, Mukraj D. Internal sphincterotomy is superior to topical nitroglycerin in the treatment of chronic anal fissure. *Diseases of the colon & rectum*. 2000 Aug 1;43(8):1048-55.
14. Knight JS, Birks M, Farouk R. Topical diltiazem ointment in the treatment of chronic anal fissure. *British journal of surgery*. 2001 Apr;88(4):553-6.
15. MacDonald A, Smith A, McNeill AD, Finlay IG. Manual dilatation of the anus. *British journal of surgery*. 1992 Dec;79(12):1381-2.
16. Nielsen MB, Rasmussen OØ, Pedersen JF, Christiansen J. Risk of sphincter damage and anal incontinence after anal dilatation for fissure-in-ano. *Diseases of the colon & rectum*. 1993 Jul 1;36(7):677-80.
17. Eisenhammer S. The evaluation of the internal anal sphincterotomy operation with special reference to anal fissure. *Surgery, gynecology & obstetrics*. 1959 Nov;109:583.
18. Garcia-Aguilar J, Belmonte Montes C, Perez JJ, Jensen L, Madoff RD, Wong WD. Incontinence after lateral internal sphincterotomy: anatomical and functional evaluation. *Dis Colon Rectum*. 1998;41:423–427.
19. Khubchandani IT, Reed JF. Sequelae of internal sphincterotomy for chronic fissure in ano. *British journal of surgery*. 1989 May 1;76(5):431-4.
20. Hsu TC, MacKeigan JM. Surgical treatment of chronic anal fissure: a retrospective study of 1753 cases. *Dis Colon Rectum*. 1984;27:475–478.

21. Madoff RD, Fleshman JW. AGA technical review on the diagnosis and care of patients with anal fissure. *Gastroenterology*. 2003;124:235–245. doi: 10.1053/gast.2003.500.
22. Notaras MJ. The treatment of anal fissure by lateral subcutaneous internal sphincterotomy—a technique and results. *British Journal of Surgery*. 1971 Feb 1;58(2):96-100.
23. Abcarian H. Surgical correction of chronic anal fissure: results of lateral internal sphincterotomy vs. fissurectomy—midline sphincterotomy. *Diseases of the Colon & Rectum*. 1980 Jan 1;23(1):31-6.
24. Mousavi SR, Sharifi M, Mehdikhah Z. A comparison between the results of fissurectomy and lateral internal sphincterotomy in the surgical management of chronic anal fissure. *Journal of Gastrointestinal Surgery*. 2009 Jul 1;13(7):1279-82.
25. Nelson RL. Meta-analysis of operative techniques for fissure-in-ano. *Diseases of the colon & rectum*. 1999 Nov 1;42(11):1424-8.
26. Scholz T, Hetzer FH, Dindo D, Demartines N, Clavien PA, Hahnloser D. Long-term follow-up after combined fissurectomy and Botox injection for chronic anal fissures. *International journal of colorectal disease*. 2007 Sep 1;22(9):1077-81.
27. Aoki KR, Guyer B. Botulinum toxin type A and other botulinum toxin serotypes: a comparative review of biochemical and pharmacological actions. *European Journal of Neurology*. 2001 Nov;8:21-9.
28. Kao IN, Drachman DB, Price DL. Botulinum toxin: mechanism of presynaptic blockade. *Science*. 1976 Sep 24;193(4259):1256-8.
29. Dressler D, Saberi FA. Botulinum toxin: mechanisms of action. *European neurology*. 2005;53(1):3-9.
30. Jost WH, Schimrigk K. Use of botulinum toxin in anal fissure. *Dis Colon Rectum*. 1993;36:974.

31. Maria G, Cassetta E, Gui D, Brisinda G, Bentivoglio AR, Albanese A. A comparison of botulinum toxin and saline for the treatment of chronic anal fissure. *N Engl J Med.* 1998;338:217–220. doi: 10.1056/NEJM199801223380402.
32. Bobkiewicz A, Francuzik W, Krokowicz L, Studniarek A, Ledwosiński W, Paszkowski J, Drews M, Banasiewicz T. Botulinum toxin injection for treatment of chronic anal fissure: is there any dose-dependent efficiency? A meta-analysis. *World journal of surgery.* 2016 Dec 1;40(12):3064-72.
33. Menteş BB, Irkörücü O, Akın M, Leventoğlu S, Tatlıcıoğlu E. Comparison of botulinum toxin injection and lateral internal sphincterotomy for the treatment of chronic anal fissure. *Diseases of the colon & rectum.* 2003 Feb 1;46(2):232-7.
34. Giral A, Memişoğlu K, Gültekin Y, İmeryüz N, Kalaycı C, Ulusoy NB, Tözün N. Botulinum toxin injection versus lateral internal sphincterotomy in the treatment of chronic anal fissure: a non-randomized controlled trial. *BMC gastroenterology.* 2004 Mar 22;4(1):7.
35. Shao WJ, Li GC, Zhang ZK. Systematic review and meta-analysis of randomized controlled trials comparing botulinum toxin injection with lateral internal sphincterotomy for chronic anal fissure. *International journal of colorectal disease.* 2009 Sep 1;24(9):995-1000.
36. Netter FH. *Atlas of Human Anatomy E-Book: including NetterReference. com* Access with Full Downloadable Image Bank. Elsevier Health Sciences; 2017 Dec 19.

ANNEXURE 1: LIST OF FIGURES

Figure 1: Anatomy of Anal Canal	14
Figure 2: Anatomy of Sphincters	16
Figure 3: Innervation of Anal Canal.....	17
Figure 4: Acute vs Chronic fissure.....	20
Figure 5: Etiology of fissure in ano	22
Figure 6: Examination of anal fissure.....	24
Figure 7: Nitroglycerin ointment.....	26
Figure 8: Diltiazem ointment	27
Figure 9: Lateral Open Sphincterotomy- incision	29
Figure 10: Dissecting internal sphincter fibres	30
Figure 11: Fibres cut and wound closed if needed.....	30
Figure 12: Lateral Closed Sphincterotomy	31
Figure 13: 11 blade inserted at groove	31
Figure 14: Blade rotated through fibres	32
Figure 15: Excision of fissure	32
Figure 16: Raising of mucosal flap	33
Figure 17: Closure by mucosal flap (optional).....	33
Figure 18: Botulinum toxin molecule.....	35
Figure 19: Molecular pattern of Botulinum toxin	36
Figure 20: Mechanism of Action of Botulinum toxin	37
Figure 21: Vial of Botulinum toxin commercially available	39
Figure 22: Anal fissure in a patient	43
Figure 23: Anal fissure in another patient.....	43
Figure 24: Dissection of internal sphincter fibres	44
Figure 25: Cutting of the fibres	44
Figure 26: Reconstituted toxin with insulin syringe.....	45
Figure 27: Injection of botulinum toxin in a female patient	46
Figure 28: Injection of botulinum toxin in a male patient	46
Figure 29: Numerical Pain Scale.....	48
Figure 30: Age Distribution	52
Figure 31: Gender distribution	53
Figure 32: Gender distribution between groups	54
Figure 33: Comparison of relief of pain at 1 day	55
Figure 34: Comparison of relief of pain at 1 week.....	56
Figure 35: Comparison of return to daily activity	58
Figure 36: Comparison of healing at 6 weeks.....	60
Figure 37: Comparison of healing at 3 months	61
Figure 38: Comparison of wound infection at 1 day	62
Figure 39: Comparison of wound infection at 1 week.....	63
Figure 40: Comparison of incontinence at 6 weeks	64
Figure 41: Comparison of incontinence at 3 months.....	65
Figure 42: Number of patients having incontinence	67
Figure 43: Total recurrence.....	68
Figure 44: Recurrence at 3 months.....	68

ANNEXURE 2: LIST OF TABLES

Table 1: Jorge-Wexner Score.....	49
Table 2: Age Distribution	52
Table 3: Comparison of age.....	53
Table 4: Comparison of Gender	54
Table 5: Comparison of Pain relief at 1 day	56
Table 6: Comparison of pain relief at 1 week	57
Table 7: Comparison of return to daily activities	58
Table 8: Comparison of Return to daily activities.....	59
Table 9: Comparison of healing at 6 weeks	60
Table 10: Comparison of healing at 3 months	61
Table 11: Comparison of wound infection at 1 day	62
Table 12: Comparison of wound infection at 1 week.....	63
Table 13: Comparison of Incontinence at 6 weeks.....	65
Table 14: Comparison of Incontinence at 3 months	66
Table 15: Comparison of recurrence at 3 months	69

ANNEXURE 3: INFORMATION SHEET

TITLE : “COMPARATIVE STUDY OF BOTULINUM TOXIN INJECTION AND LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT OF CHRONIC ANAL FISSURE”

Name of Investigator : Dr.CHETNA RAVINDRA.

Name of Participant :

Purpose of Research : To compare botulinum toxin injection with the gold standard treatment, lateral internal sphincterotomy in the treatment of chronic anal fissure

Study Design : Randomised Control Trial

Study Procedures : Patients will be randomly divided into two groups- one undergoing surgical sphincterotomy and the other undergoing botulinum toxin injection

Possible Risks : No risks to the patient

Possible benefits

To patient : Relief of chronic pain, and thereafter treatment of fissure via either the procedures.

Patients will be able to understand and plan their management as per their requirements

To doctor & to other people : If this study gives positive results, it can help in establishing a treatment modality which is non surgical and additionally an outpatient procedure. This will help in providing alternate treatment modalities to other patients in future.

Confidentiality of the information obtained from you : The privacy of the patients in the research will be maintained throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared

Can you decide to stop participating in the study : Taking part in this study is voluntary. You are free to decide whether to participate in this study or to withdraw at any time

How will your decision to not participate in the study affect you : Your decision will not result in any loss of benefits to which you are otherwise entitled.

Signature of Investigator

Signature of Participant

Date :

Place :

ANNEXURE 4: PATIENT CONSENT FORM

Study Detail : **“COMPARATIVE STUDY OF BOTULINUM TOXIN INJECTION AND LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT OF CHRONIC ANAL FISSURE”**

Study Centre : Rajiv Gandhi Government General Hospital, Chennai.

Patient's Name :

Patient's Age :

In Patient Number :

Patient may check () these boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask question and all my questions and doubts have been answered to my complete satisfaction.

I understand that my participation in the study is voluntary and that I am free to withdraw at any time without giving reason, without my legal rights being affected.

I understand that sponsor of the clinical study, others working on the sponsor's behalf, the Ethics committee and the regulatory authorities will not need my permission to look at my health records, both in respect of current study and any further research that may be conducted in relation to it, even if I withdraw from the study I agree to this access. However, I understand that my identity will not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from this study.

I agree to take part in the above study and to comply with the instructions given during the study and faithfully cooperate with the study team and to immediately inform the study staff if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

I hereby consent to participate in this study

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests and to undergo treatment

Signature/thumb impression

Patient's Name and Address:

Signature of Investigator

Study Investigator's Name:

Dr. CHETNA RAVINDRA,

ANNEXURE 5: QUESTIONNAIRE

PATIENT DETAILS:

Name:

Age:

Sex:

IP No. :

ON ADMISSION:

MAIN COMPLAINTS:

DURATION OF HISTORY:

ASSOCIATED COMPLAINTS:

CLINICAL EXAMINATION:

Pulse:

BP:

RR:

Temp:

Pallor:

Icterus:

CVS:

RS:

P/A:

CNS:

INVESTIGATIONS:

CBC/RFT			
TC		LFT	
DC		Total Bili	
Hb %		Dir. Bili	
PCV		SGOT	
RBC		SGPT	
Platelets		Total Protein	
Glucose		Sr. Albumin	
Urea		Na ⁺ /K ⁺	
Creatinine			

CXR:

Abdomen X-ray:

TREATMENT

OPERATIVE MANAGEMENT: METHOD USED

- Botulinum toxin
- Lateral anal sphincterotomy

Intra Op findings:

Post op Period:

FOLLOW UP:

Pain Relief:

Wound Infection:

Healing of Fissure:

Incontinence Score:

Recurrence:

ANNEXURE 6: ETHICAL COMMITTEE APPROVAL

INSTITUTIONAL ETHICS COMMITTEE MADRAS MEDICAL COLLEGE, CHENNAI 600 003

EC Reg.No.ECR/270/Inst./TN/2013
Telephone No.044 25305301
Fax: 011 25363970

CERTIFICATE OF APPROVAL

To
Dr.Chetna Ravindra
I Year Post Graduate in MS General Surgery
Institute of General Surgery
MMC/Chennai

Dear Dr.Chetna Ravindra,

The Institutional Ethics Committee has considered your request and approved your study titled "**COMPARATIVE STUDY OF BOTULINUM TOXIN INJECTION AND LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT OF CHRONIC ANAL FISSURE**" - NO.39122017

The following members of Ethics Committee were present in the meeting hold on **12.12.2017** conducted at Madras Medical College, Chennai 3

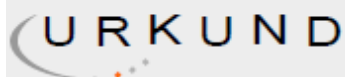
- | | |
|--|----------------------|
| 1. Prof.P.V.Jayashankar | :Chairperson |
| 2. Prof.R.Narayana Babu,MD.,DCH., Dean,MMC,Ch-3 | : Deputy Chairperson |
| 3. Prof.Sudha Seshayyan,MD., Vice Principal,MMC,Ch-3 | : Member Secretary |
| 4. Prof.N.Gopalakrishnan,MD,Director,Inst.of Nephrology,MMC,Ch | : Member |
| 5. Prof.S.Mayilvahanan,MD,Director,Inst. of Int.Med,MMC, Ch-3 | : Member |
| 6. Prof.A.Pandiyaraj,Director, Inst. of Gen.Surgery,MMC | : Member |
| 7. Prof.Shanthy Gunasingh, Director, Inst.of Social Obstetrics,KGH | : Member |
| 8. Prof.Rema Chandramohan,Prof.of Paediatrics,ICH,Chennai | : Member |
| 9. Prof. Susila, Director, Inst. of Pharmacology,MMC,Ch-3 | : Member |
| 10.Prof.K.Ramadevi,MD., Director, Inst. of Bio-Chemistry,MMC,Ch-3 | : Member |
| 11.Prof.Bharathi Vidya Jayanthi,Director, Inst. of Pathology,MMC,Ch-3: | Member |
| 12.Thiru S.Govindasamy, BA.,BL,High Court,Chennai | : Lawyer |
| 13.Tmt.Arnold Saulina, MA.,MSW., | :Social Scientist |
| 14.Thiru K.Ranjith, Ch- 91 | : Lay Person |

We approve the proposal to be conducted in its presented form.

The Institutional Ethics Committee expects to be informed about the progress of the study and SAE occurring in the course of the study, any changes in the protocol and patients information/informed consent and asks to be provided a copy of the final report.

Member Secretary - Ethics Committee

ANNEXURE 7: PLAGIARISM CERTIFICATE



Urkund Analysis Result

Analysed Document: Thesis_plagiarism.docx (D57361994)
Submitted: 10/21/2019 12:51:00 PM
Submitted By: chetnaravindra@gmail.com
Significance: 5 %

Sources included in the report:

thesis plagiarism.docx (D42409390)
Shahid161019.doc (D57111521)
mani urkund.docx (D42688487)
https://www.researchgate.net/publication/8664419_Botulinum_toxin_injection_versus_lateral_internal_sphincterotomy_in_the_treatment_of_chronic_anal_fissure_A_non-randomized_controlled_trial
<https://www.sciencedirect.com/topics/immunology-and-microbiology/anal-canal>
https://www.researchgate.net/publication/6126546_Subcutaneous_Fissurotomy_A_Novel_Procedure_for_Chronic_Fissure-in-ano_A_Review_of_109_Cases
https://www.researchgate.net/publication/11633033_Progress_in_the_understanding_and_treatment_of_chronic_anal_fissure

Instances where selected sources appear:

19

10/21/2019

Gmail - [Urkund] 5% similarity - chetnaravindra@gmail.com



chetna ravindra <chetnaravindra@gmail.com>

[Urkund] 5% similarity - chetnaravindra@gmail.com

1 message

report@analysis.orkund.com <report@analysis.orkund.com>
To: chetnaravindra@gmail.com

Mon, Oct 21, 2019 at 4:44 PM

Document sent by: chetnaravindra@gmail.com
Document received: 10/21/2019 12:51:00 PM
Report generated 10/21/2019 1:14:30 PM by Urkund's system for automatic control.

Student message: Sending my thesis for anti-plagiarism check

Document : Thesis_plagiarism.docx [D57361994]

About 5% of this document consists of text similar to text found in 108 sources. The largest marking is 69 words long and is 98% similar to its primary source.

PLEASE NOTE that the above figures do not automatically mean that there is plagiarism in the document. There may be good reasons as to why parts of a text also appear in other sources. For a reasonable suspicion of academic dishonesty to present itself, the analysis, possibly found sources and the original document need to be examined closely.

Click here to open the analysis:
<https://secure.orkund.com/view/55767823-623604-464083>

Click here to download the document:
<https://secure.orkund.com/archive/download/57361994-551608-385324>

CERTIFICATE – II

This is to certify that this dissertation work titled “**COMPARATIVE STUDY OF BOTULINUM TOXIN INJECTION AND LATERAL INTERNAL SPHINCTEROTOMY IN THE TREATMENT OF CHRONIC ANAL FISSURE**” of the candidate **Dr. CHETNA RAVINDRA** with Registration Number **221711005** for the award of **M.S degree** in the BRANCH -1 of **General Surgery**. I personally verified the urkund.com website for the purpose of plagiarism Check. I found that the uploaded thesis file contains from introduction to conclusion pages and result shows **5 %** percentage of plagiarism in the dissertation.

Guide & Supervisor sign with Seal.

ANNEXURE 8: MASTER CHART

Case:

S No	Age	Sex	Relief of pain at 1 day	Pain Score at 1 week	Relief of Pain at 1 week	Pain Score at 1 week	Return to daily activities at POD	Return to daily activity <3 days	Healing of fissure at 6 weeks	Healing of fissure at 3 months	Wound infection at 1 day	Wound infection at 1 week	Incontinence at 6 weeks	Wexner Score at 6 weeks	Incontinence at 3 months	Wexner score at 3 months	Recurrence at 3 months
1	35	M	Yes	0	Yes	0	1 day	Yes	Yes	Yes	No	No	No	0	No	0	No
2	40	F	Yes	0	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
3	26	M	No	2	Yes	2	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
4	28	M	No	3	Yes	3	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
5	37	M	Yes	0	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
6	30	F	No	4	Yes	4	2 days	Yes	Yes	Yes	No	Yes	Yes	4	Yes	3	No
7	29	M	No	5	Yes	5	2 days	Yes	No	Yes	No	No	No	0	No	0	No
8	42	M	Yes	0	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
9	41	F	Yes	0	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
10	36	F	No	4	Yes	4	3 days	No	Yes	Yes	No	No	No	0	No	0	No
11	48	M	No	4	Yes	4	3 days	No	Yes	Yes	No	No	No	0	No	0	No
12	45	M	Yes	0	Yes	0	2 days	Yes	No	Yes	No	No	No	0	No	0	No
13	46	M	No	6	Yes	6	2 days	Yes	No	Yes	No	No	No	0	No	0	No
14	37	M	No	3	Yes	3	2 days	Yes	No	Yes	No	No	No	0	No	0	No
15	33	F	No	2	Yes	2	3 days	No	Yes	Yes	No	No	No	0	No	0	No
16	28	M	No	1	Yes	1	2 days	Yes	Yes	Yes	No	Yes	Yes	2	No	0	No
17	29	M	Yes	0	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
18	31	F	No	2	Yes	2	2 days	Yes	No	Yes	No	No	No	0	No	0	No
19	35	M	Yes	0	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
20	33	F	No	3	Yes	3	2 days	Yes	No	Yes	No	No	No	0	No	0	No
21	34	F	No	3	Yes	3	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
22	29	M	No	2	Yes	2	1 day	Yes	Yes	Yes	No	No	No	0	No	0	No
23	39	M	Yes	0	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
24	41	F	No	1	Yes	1	3 days	No	No	No	No	No	No	0	No	0	Yes
25	32	M	No	1	Yes	1	1 day	Yes	Yes	Yes	No	No	No	0	No	0	No
26	35	M	Yes	0	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
27	32	F	No	1	Yes	1	3 days	No	Yes	Yes	No	No	No	0	No	0	No
28	36	M	Yes	0	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
29	29	F	Yes	0	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
30	42	M	No	1	Yes	1	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No

Control:

S No	Age	Sex	Relief of pain at 1 day	Pain Score	Relief of Pain at 1 week	Pain Score	Return to daily activities at POD	Return to daily activity <3 days	Healing of fissure at 6 weeks	Healing of fissure at 3 months	Wound infection at 1 day	Wound infection at 1 week	Incontinence at 6 weeks	Wexner Score at 6 weeks	Incontinence at 3 months	Wexner score at 3 months	Recurrence at 3 months
1	26	M	No	4	Yes	0	2 days	Yes	Yes	Yes	No	No	Yes	7	Yes	3	No
2	31	M	No	5	Yes	0	4 days	No	Yes	Yes	No	No	No	0	No	0	No
3	33	F	Yes	0	Yes	0	1 day	Yes	Yes	Yes	No	No	No	0	No	0	No
4	27	M	No	5	Yes	0	5 days	No	Yes	Yes	Yes	No	Yes	4	No	0	No
5	30	M	No	4	Yes	0	5 days	No	Yes	Yes	No	Yes	No	0	No	0	No
6	34	F	No	3	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
7	33	F	No	3	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
8	30	M	No	6	Yes	0	2 days	Yes	Yes	Yes	No	No	Yes	4	No	0	No
9	33	F	No	6	No	2	7 days	No	No	Yes	No	No	No	0	No	0	No
10	36	M	No	3	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
11	36	F	No	4	Yes	0	4 days	No	Yes	Yes	No	No	No	0	No	0	No
12	37	M	No	3	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
13	39	F	No	5	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
14	42	M	No	5	No	3	6 days	No	No	Yes	No	No	No	0	No	0	Yes
15	44	F	No	3	Yes	0	3 days	No	Yes	Yes	No	No	Yes	6	Yes	3	No
16	46	M	No	2	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
17	29	F	No	2	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
18	34	F	No	1	Yes	0	5 days	No	Yes	Yes	Yes	Yes	Yes	3	No	0	No
19	40	F	No	3	Yes	0	5 days	No	Yes	Yes	No	No	No	0	No	0	No
20	29	M	No	2	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
21	35	M	No	3	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
22	36	M	No	3	Yes	0	4 days	No	Yes	Yes	No	No	Yes	4	Yes	2	No
23	32	F	No	4	No	2	7 days	No	Yes	Yes	No	No	No	0	No	0	No
24	31	F	No	3	Yes	0	4 days	No	Yes	Yes	No	No	No	0	No	0	No
25	40	F	No	5	No	3	6 days	No	No	Yes	No	No	Yes	3	No	0	No
26	24	M	Yes	0	Yes	0	1 day	Yes	Yes	Yes	No	No	No	0	No	0	No
27	28	M	No	2	Yes	0	2 days	Yes	Yes	Yes	No	No	No	0	No	0	No
28	35	M	No	3	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
29	37	M	No	2	Yes	0	3 days	No	Yes	Yes	No	No	No	0	No	0	No
30	39	F	No	4	No	2	6 days	No	Yes	Yes	No	No	Yes	6	No	0	No