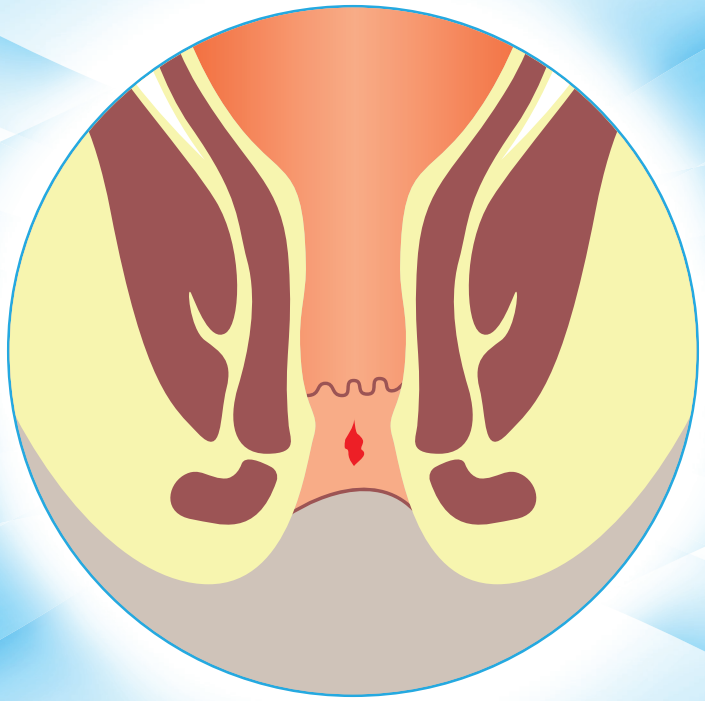
The Association of Colon and Rectal Surgeons of India
(A Section of ASI)



FISSURE IN ANO

PRACTICE GUIDELINES 2021

The Association Of Colon And Rectal Surgeons Of India

Practice Parameters Consensus Meeting - 11th Nov 2021, Hotel Renaissance Mumbai

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Foreword

Disorders of the colon and rectum are not only very common but complex too and many a time difficult to treat. The urge to provide best treatment amongst the vast majority available is even more perplexing and frustrating at times. This gets further compounded by the lack of supporting evidences locally. Our members are more guided by evidences produced by other part of the world though it is a well known fact that colorectal disorder occurrences, behaviour and treatment responses may differ across the continents. A need was therefore felt to compile various available literature for some common colorectal disorders and produce them in the form of Practice Guidelines suitable for our members. It is an established fact that treatment modalities guided by the explicit, careful and judicious use of the best evidence available serves as a guide for most appropriate clinical decision making and patient care.

The Association of Colon and Rectal Surgeons of India lead by its team of expert faculties in their respective fields have done some excellent literature search and collated the available experiences to prepare this guidelines for you. We hope this will serve as a ready reckoner for our members in their times of need and help them to combat many litigations too.

I take this opportunity to thank all the contributors for their constant support in this endeavour.

Dr. Niranjan Agarwal
President-ACRSI

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FISSURE IN ANO

PRACTICE GUIDELINES 2021

Summary of recommendations

Management of Acute Anal Fissure

1) Conservative management of acute anal fissures

- Non-operative measures like sitz bath, high-fiber diet with or without topical anesthetic agents should be recommended as the first-line treatment for acute anal fissures. (Strong recommendation based on moderate-quality evidence, 1B)

2) Medical management of acute anal fissure

- Chemical sphincterotomy agents are indicated in acute and chronic anal fissure and where conservative treatment with stiz bath, fibres and topical anesthetic have failed (Strong recommendation based on high-quality evidence, 1A)
- Topical nitrates can be used to treat anal fissure but it is not available in India now. Severe headache leading to poor compliance by the patientand non-availability of the drug limits its use. (Strong recommendation based on high-quality evidence, 1A)
- Calcium channel blockers (Diltiazem and Nifedipine) may be used as the first-line treatment of acute and chronic anal fissure. They have fewer adverse effects, and are well tolerated with increased healing rate and low recurrence rate. (Strong recommendation based on high-quality evidence, 1A)
- Botulinum Toxin can be considered as a safe and effective treatment for anal fissures resistant to medical treatment and before offering surgical option. The dose, site and technique of injection has less implications on the outcome. (Strong recommendation based on low- and very-low-quality evidence, 1B)

3) Surgical management of chronic anal fissure

- Lateral internal sphincterotomy is recommended as a second-line therapy following failure of first-line medical management. (Strong recommendation based on high-quality evidence, 1A)
- Lateral internal sphinceterotomy may be considered as first-line treatment in select patients suffering from severe pain and spasm, who are are expected to be non-compliant to medical management, and with low risk for incontinence. (Weak recommendation based on low- quality quality evidence, 2C)
- Open and closed techniques of LIS have similar efficacy. Therefore, either technique can be recommended for treatment of CAF. (Strong recommendation based on high-quality evidence, 1A)
- Tailored LIS (tailored to the length of the fissure) shows similar-to-worse healing rates with low rate of incontinence compared to conventional (LIS). (Weak recommendation based on moderate-quality evidence, 2B)
- Lateral internal sphincterotomy has higher healing rates and lower rate of recurrence and incontinence when compared to fissurectomy and anal dilatation. (Strong recommendation based on high-quality evidence, 1A)
- Anocutaneous flap may be recommended as a sphincter-preserving alternative to LIS as it has lower rates of incontinence but inferior healing rates. (Weak recommendation based on moderate-quality evidence, 2B)
- We do not recommend manual anal dilatation. (Strong recommendation based on moderate-quality evidence, 2B)

4) Managing fissures in special conditions

- Fissure in children should be treated initially by conservative measures. Failure of conservative measures should be an indication for medical management with local GTN or calcium channel blockers. Lateral sphincterotomy or fissurectomy should be reserved for those failing to heal with medical treatment (Strong recommendation based on low- and very-low-quality evidence, 1C).
- Fissure in ano secondary to anal tuberculosis, HIV or Crohn's disease should be managed medically, with concurrent treatment for the primary systemic disease. Surgical intervention should be limited to obtaining tissue for histopathological diagnosis and to drain any purulent collection. (Strong recommendation based on low quality evidence, 1C).
- Fissure in ano during pregnancy and after childbirth should be managed by conservative methods, as they tend to have low pressure sphincter tone. If the fissure persists and become chronic, surgical treatment by excision of the fissure with an anal advancement flap should be considered. (Weak recommendation with low quality evidence, 2C)

Introduction

Anal fissure is longitudinal tear in the squamous epithelium of the anal canal extending from anal verge cephalad often up to the dentate line. Anal fissure is one of the common anorectal disorders. It is characterized by debilitating pain both during and after defecation and lasting for few hours.(1, 2) This feature helps distinguish anal fissures from other disorders that cause anal pain such as perianal and ischiorectal abscesses, thrombosed hemorrhoids, viral ulcers, etc.(2) Patients with fissures in lateral locations within the anal canal, and those with multiple fissures are considered to be atypical and need careful evaluation due to their probable association with other etiologies are like IBD, HIV infection, hematologic malignancies and tuberculosis.(3)

The annual incidence rate of anal fissure is 1.1 per 1000 person-years and is equivalent to an average lifetime risk of 7.8%.(4) The incidence of anal fissure in Indian studies was in the range of 16%-36% in patients presenting with anorectal complaints.(5-9) Etiology of fissure remains unclear; however, fissures associated with internal anal sphincter hypertonia are probably ischemic in nature. Risk factors for anal fissures include chronic constipation, frequent defaecation and diarrhea, obesity, and hypothyroidism. Fissures may sometimes present with anorectal bleeding, and this can lead to misdiagnosis of symptomatic hemorrhoids.

Based on the chronicity and morphological appearance, fissures are classified as acute and chronic. Acute fissures involveonly the superficial mucosal layer that is well demarcated and fresh without visible internal anal sphincter (IAS) fibers. Fissure is separated by longitudinal muscle from IAS. Acute fissures appear as a longitudinal tear. Anal fissures of > 8 weeks duration presenting with distinct anatomical features such as visible IAS fibers at the fissure base along with a hypertrophied anal papilla, sentinel pile and indurated margins are classified as chronic fissures. Acute fissures mostly heal spontaneously. Whereas the hypertrophy of IAS fibers keep the wound open preventing spontaneous wound healing and fissure becomes chronic. Due to embarrassment felt by patients owing to the location of the symptoms, they may present to care late in the course of their illness.

The management options include general measures such as increased intake of dietary fibers, adequate fluid intake, topical anesthetics, and medical treatments such as glyceryl trinitrate (GTN) ointment, calcium channel blockers (CCB) e.g. diltiazem and nifedipine cream; and botulinum toxin. Surgical options include lateral sphincterotomy, advancement flap procedures and fissurectomy. This consensus statement recommends evidence-based practice for managing fissures in the Indian population.

Methodology

An organized literature search was performed in PubMed, the Cochranedatabase of collected reviews, and Google scholar. Apart from these, resources of regulatory bodies, guidelines and recommendations of international societies were also searched. Search was restricted to articles and abstracts published in English. Keywords included were “anal fissure”, “fissure-in-ano”, “anal fissure AND nitroglycerin”, “anal fissure AND nitrates”, “analfissure AND diltiazem”, “anal fissure AND nifedipine”, “analfissure AND fiber”, “anal fissure AND botulinum”, “anal fissure AND sphincterotomy” and “anal fissure AND flap”. Prospective, randomized, controlled trials and meta-analyses were given preference in developing this practice parameters. The draft guidelines were shared with the expert committee members through email and a consensus was reached during a consensus meeting over video conferencing. A method adopted by American Society of Colon and Rectal Surgeons (ASCRS) was used to derive quality of evidence, wherein 1 was assigned to strong recommendation and 2 was assigned to weak recommendations. These recommendations were again categorized based on the level of evidence as A for RCTs without important limitations or overwhelming evidence from observational studies, B for RCTs with important limitations (inconsistent results, methodologic flaws, indirect or imprecise) or exceptionally strong evidence from observational studies, and C for observational studies or case series or consensus opinion of the expert group (Table 1).(10)

Table 1 The GRADE system for grading recommendations (10)

Supporting evidence	Quality of evidence	Grade of recommendation	Quality of evidence
RCTs without important limitations or overwhelming evidence from observational studies	Benefits clearly outweigh risk and burdens or vice versa	1	A
	Benefits closely balanced with risks and burdens	2	A
RCTs with important limitations (inconsistent results, methodologic flaws, indirect, or imprecise) or exceptionally strong evidence from observational studies	Benefits clearly outweigh risk and burdens or vice versa	1	B
	Benefits closely balanced with risks and burdens	2	B
Observational studies or case series or consensus opinion of the panel	Benefits clearly outweigh risk and burdens or vice versa	1	C
	Uncertainty in the estimates of benefits, risks and burden; benefits, risks, and burden may be closely balanced	2	C

Management of Acute Anal Fissure

1. Conservative management of acute anal fissures

Acute anal fissures are managed conservatively by non-operative options like a sitz bath, psyllium fiber or bulking agents with or without topical anesthetics.

In a prospective randomized study, proportion of patients achieving symptom relief was higher ($P < 0.05$) in those treated with sitz baths and bran (87%) compared to those on hydrocortisone (82.4%) and lignocaine (60%).(11) In a double-blind, placebo-controlled trial in patients with recently healed acute posterior anal fissures, the recurrence was significantly lower in those treated with bran 5 g three times daily (16%) compared to placebo ($P < 0.01$).(12) Some relatively old retrospective studies that included 393 and 876 patients and 5 years of follow-up,showedhealing rates of up to ~ 45% with medical therapy alone.(13, 14) Recently, in a small prospective study, conservative treatment with bulking agents, sitz baths along with topical therapy, significantly improved the healing rate and pain relief in acute fissures more efficiently compared to CAF; and the healing rates decreased proportionately with increased duration of complaint. Allthese interventions were well-tolerated and no side-effects were observed.(15)

Passage of large bulky stools will also result in direct trauma from stretching of the anal mucosa leading to anal fissures. With the development of chronic fissure, secondary anal sphincter spasm with resultant anodermal ischaemia, it does not make sense to further worsen the spasm by trying to force large bulky stools through the anus. It is therefore recommended to use osmotic and stimulant laxatives for management of hard stools.(16)

Summary of studies from India

In a prospective study, both warm sitz bath (N = 25) and warm sitz shower bath (N = 25) were found to significantly improve symptoms in patients with anal fissures.(17) In another prospective study, warm sitz bath in addition to analgesics and high-fiber diet resulted in a significant reduction in pain scores, greater improvement in symptoms and patient satisfaction scores compared to analgesics, and high-fiber diet alone.(18) In a prospective study by Gupta et al., sitz baths significantly improved patient satisfaction scores in acute anal fissures; however the pain scores were found to improve only numerically. (19)

ACRSI Recommendation

- Non-operative measures like sitz bath, high-fiber diet with or without topical anesthetic agents should be recommended as the first-line treatment for acute anal fissures. (Strong recommendation based on moderate-quality evidence, 1B)

2. Medical management of acute anal fissure

It is essential to note that virtually all operations and therapeutics used in treating anal fissures are typically designed to treat chronic fissures. A typical treatment plan aims to address the pain that occurs due to traumatic passing of stool, abnormal defecation pattern, e.g. excessive straining; and decreasing anal sphincter tone and local ischemia in patients with a hypertonic sphincter.

Pharmacologic agents commonly used for medical management by chemical sphincterotomy are topical glyceryl trinitate (GTN) calcium channel blockers such as diltiazem and nifedipine and botulinum toxin. Chemical sphincterotomy agents are indicated in chronic anal fissure and in acute anal fissure where conservative treatment with sitz bath, dietary fibers, and topical ananesthetic failed. They should be used for 2-3 times a day for eight weeks to a maximum of 12 weeks. They should be stopped if patient develop any adverse effects. If there is no improvement with the use of chemical sphincterotomy agents after its use for three months, it should be stopped. The chemical sphincterotomy agents available in India are calcium channel blockers, diltiazem 2%, nifedipine 0.3% with lidocaine 1.5%, and botulinum toxin. For optimal results, adequate dose at regular intervals for periods over six to eight weeks, or as advised by the surgeons is very important. In few cases fissure may present without symptoms, but it would not have healed completely. In those cases if the patient stops the treatment early due to symptomatic relief, the fissure can recur. Therefore, patients should be advised to strictly follow their surgeon's advice.

a. Topical Glyceryltrinitrate (GTN)

GTN acts as a nitric oxide donor when applied topically in the anal canal. Nitric oxide is a neurotransmitter which mediates the relaxation of the internal anal sphincter. GTN diffuses through the mucosa and causes reduction in the internal sphincter pressure and increases the blood flow by its vasodilatory effect and there by promote healing of the fissure. Topical GTN is effective in healing 46% to 70% of chronic anal fissure.(20-25) The prime adverse effect is severe headache, with an incidence which varies from 29% to 72% of the patients.(20-23, 26, 27) The severe headache leads to discontinuation of treatment in about 3% to 20% of patients.(28) On long term follow up, the symptoms of fissure-in ano may recur in 15% to 63% of patients, which is very high when compared to sphincterotomy.(27, 29-31) GTN is inferior to Botulinum toxin / lateral internal sphincterotomy and calcium channel blocker.(30, 31) However, GTN is no longer available for use in India.

b. Calcium channel blockers/ antagonists

Internal anal sphincter cell contraction mainly depends on the intracellular calcium ions level. The calcium channel blockers like Diltiazem and Nifedipine cause smooth muscle relaxation and vasodilatation, thus promoting healing of the anal fissure. Topical application of these drugs lowers the resting anal pressure and relieves pain and promotes healing of the fissure. The healing rate of anal fissures is 65% - 95% with topical calcium channel blockers.(32, 33)

The healing rate of chronic anal fissure increases with increasing frequency of application of topical calcium channel blocker. Calcium channel blocker through topical application is the preferred mode of treatment for chronic anal fissure. On long term follow up studies, similar recurrence rates were noted for calcium channel blockers and GTN.(34)

Diltiazem 2% gel is applied topically, intra-anally twice or thrice daily for six to eight weeks. The topical cream application is done by the patient, using the tip of the index finger, to just inside the anal canal and 1 cm around the anus circumferentially. Healing rate is 49%.(23) Incidence of adverse effects, especially headache, are lower, when compared to GTN. 2% topical diltiazem hydrochloride was more effective than 0.2% topical glyceryl trinitrate. Other adverse effects which occur are perianal itching which may become troublesome, drowsiness and mood swings.

Nifedipine 0.3% with lidocaine 1.5% cream can be used twice or thrice a day for 6 to 8 weeks achieving healing rate of 94.5%.(35) The combination of nifedipine and lidocaine offers reduction in pain and promotes healing. A modified small nozzle formulation is available for nifedipine offering ease of application and exact dosing.

When the efficacy of GTN, calcium channel blockers-diltiazem and nifedipineis compared, all have healing rates which are almost similar. But CCB's have fewer adverse effects, when compared to GTN.(29) We could not find any randomized comparative study comparing efficacy of diltiazem and nifedipine. However, a recent prospective study showed similar efficacy and safety for nifedipine and diltiazem.(36) CCB's can be used as first-line treatment for chronic anal fissure since they are very effective with fewer or negligible side effects.(37)

Lateral Internal Sphincterotomy (LIS) has shown higher healing rate (88.2% to 100%) compared to nifedipine (68.9% to 96.7%) and diltiazem (71%) in randomized controlstudies.(38-40) Several Indian studies have also shown higher healing rate, better pain relief and low recurrence rates with LIS.(41-47) CCBs could be an initial treatment in patients unwilling or unfit for LIS or as a bridge therapy till sphincterotomy can be planned.

c. Botulinum toxin

Botulinum Toxin (BTX) is a type of chemical sphincterotomy which acts by blocking sympathetic response, causing relaxation of the sphincter muscle spasm & reducing sphincter tone thus resulting in healing of Anal fissure.

BTX is indicated after failure of 3 weeks of conservative management and before offering surgery to the patient. Though it can be done as an OPD procedure, it is safer to adopt a day care approach with short GA to avoid accidental injection into the External Anal Sphincter (EAS) or the Puborectalis sling that can lead to continence related complications. It is recommended to be injected in distal half of Internal Anal Sphincter (IAS) and away from the fibrous edges, on either side of the Anal fissure. Injecting at more than two sites has shown no additional benefits.

Dosage of 20 to 40 units have shown to give successful results in 60% to 88% whereas higher doses have not proved additionally beneficial but rather increase the chances of fecal incontinence.(48)

The majority of published studies that evaluate the use of botulinum toxin involve comparisons with

nitroglycerin. A Cochrane systematic review found botulinum toxin to be equally effective as GTN but showed lower incidence of headache.(29) Similar findings were confirmed in a meta-analysis by Sahebally, where a random effects analysis showed no significant differences in incomplete fissure healing (OR 0.47, 95% CI: 0.13–1.68, *P* = 0.24) or recurrence (OR 0.70, 95% CI 0.39–1.25, *P* = 0.22) between botulinum toxin and GTN.(49) The overall fissure healing rate of BTX injection has been estimated at 65% in a Cochrane review and a meta-analysis by Boland et al. showing fissure healing rate of 66.7%.(50) Synergistic benefits are shown when BTX and chemical agents were used together. Multiple randomized studies shows superiority of lateral internal sphincterotomy (LIS) over botulinum toxin for CAF and should be considered in failed or recurrent cases after BTX treatment.(51-58) BTX with Fissurectomy may be effective, but there is no current evidence to support the same.

Local and systemic adverse effects are noted, but are rarely mentioned in published literature. Though transient reversible incontinence to flatus (10%) & faeces (5%) occurs after BTX treatment, the incidence is less than that of the reported permanent incontinence that can occur after LIS. It would be prudent to avoid BTX treatment in children, during pregnancy and lactation as there is no evidence to support its safety and efficacy in these patient groups.

Summary of studies from India

A prospective randomized study by Kaistha et al. showed botulinum toxin injection (BOTOX) significantly reduces pain in patients with CAF as compared to Lord's procedure (VAS score pre-operative to 4 weeks post-operative:7.40 ± 1.66 to 0.00 ± 0.00; *P* < 0.001 vs. 7.92 ± 1.29 to 0.24 ± 0.52; *P* < 0.001; *P* = 0.013 BOTOX vs. Lords').(59) Improvement in the spasm of internal anal sphincter was also seen with BOTOX during 4-6 weeks follow-up. In another study by Rehan et al, botulinum injections were used as first line treatment in 50 patients, including both acute and chronic fissure showed that > 50% patients relieved from symptoms and 40% healed at 3rd week, with 93% healing rate and 74% symptom relief noted within 3 months.(60) In another study by Mehrotra, in 30 patients with chronic anal fissure treated with botulinum toxin injection into internal sphincter had significant symptomatic relief of pain (73.3%) with high rates (93.3%) of fissure healing at 3 months.(61) Although these studies suggest that botulinum injection can be used as the first line of management for acute and chronic uncomplicated anal fissures, there were no control or comparison groups and lack long term follow-up data.

ACRSI Recommendations on medical management

- Chemical sphincterotomy agents are indicated in acute and chronic anal fissure and where conservative treatment with stiz bath, fibres and topical anesthetic have failed (Strong recommendation based on high-quality evidence, 1A)
- Topical nitrates can be used to treat anal fissure but it is not available in India now. Severe headache leading to poor compliance by the patientand non-availability of the drug limits its use. (Strong recommendation based on high-quality evidence, 1A)
- Calcium channel blockers Diltiazem and Nifedipine may be used as the first-line treatment of acute and chronic anal fissure. They have fewer adverse effects, and are well tolerated with increased healing rate and low recurrence rate. (Strong recommendation based on high-quality evidence, 1A)
- Botulinum Toxin can be considered as a safe and effective treatment for anal fissures resistant to medical treatment and before offering surgical option. The dose, site and technique of injection has less implications on the outcome. (Strong recommendation based on low- and very-low-quality evidence, 1B)

3. Surgical management of Anal Fissure

The goals of surgical treatment are to decrease resting anal canal pressure improving the blood perfusion thus resulting in fissure healing. The indications for surgery in chronic fissure are failure of chemical sphincterotomy, patients unwilling to continue with medical management frequent recurrences of disease, large skin tags, large hypertrophied papilla, unrelenting bleeding and in case of fissure complicated by abscess, and fistula. In acute anal fissure, surgery is a choice in select patients who are unwilling for medical therapy.

a. Lateral internal sphincterotomy (LIS)

Superiority over medical therapy: The healing rate following LIS has been up to 100%. Several comparative randomized studies demonstrated the superiority of LIS in terms of higher healing rates and low recurrence rates when compared with nitrates, CCB and botulinum A. A meta-analysis by Nelson et al. showed superiority of LIS over any medical therapy with an odds ratio of 0.12 (CI 0.07–0.21).(62) Another network meta-analysis reported LIS to be most efficacious with a healing rate of 93.1% compared to dilatation (84.4%), anal flap (79.8%), botulinum toxin (62.6%) and non-invasive medical therapy (58.6%). On network meta-analysis, compared with non-invasive medical therapy, the odds ratio for healing after LIS was 9.9 (95% CI: 5.4–18.1).(63)

Based on this data, LIS can be used as a first-line option for CAF with appropriate patient selection and education. Risk factors for poor outcomes with LIS are elderly, patients with anterior fissures, prior anorectal surgery, female gender, and female with previous multiple vaginal deliveries. Although LIS has an increased risk of developing anal incontinence compared to medical therapy, the absolute risk remains low in the low-risk group.(50) Medical therapy is also associated with poor compliance in some patients and conversely the quality of life is reported to be better with LIS.(64-66)

Open vs closed LIS: The LIS can be performed by using either a closed or open technique. Open LIS involves directly opening the mucosa, exposing the internal sphincter muscle fibers and dividing them under direct vision. While in the closed technique, a blade is passed directly under the mucosa or through the intersphincteric groove prior to dividing the muscle. Several randomised controlled trials and a Cochrane systematic review confirm equal efficacy of both open and closed techniques, with an odds ratio (OR) for fissure persistence of 1.00 (95% CI:0.4–2.48) and an OR for fecal incontinence to be 0.87 (95% CI 0.41–1.83).(67) Indian studies have shown preference for closed LIS over open LIS due to higher complication rates with the open LIS.(68-70) Conversely, open LIS was found to be associated with low rates of morbidity and recurrence in female patients with CAF.(71)

Site of LIS: The vast majority of the published literature has advised the use of LIS, either at (Left lateral or right lateral). Avoidance the posterior midline IS has been recommended, because it has been associated with delayed healing and guttering of the posterior midline scar, which is called the "keyhole" deformity, which results in trapping of fecal matter and soiling. Posterolateral internal sphincterotomy (PLIS) is performed at a point midway between the standard lateral position and the posterior midline position (either at 4 o'clock or 5 o'clock) which has shown better healing, better symptom relief, low incidence of fecal incontinence, avoiding development of keyhole deformity.(72)

How much of sphincter to divide: The incontinence rate is significantly higher in patients with sphincter division extending to more than 25% of total length of the sphincter.

Partial or tailored LIS: The proximal extent of LIS is a matter of on-going debate. Dividing the internal sphincter at or just above the dentate line may lead to an excessive division of the muscle, particularly in patients with a short anal canal. But by 'tailoring' to the length of the fissure may help preserve more muscle while still promoting healing. However, comparative evidence between traditionaland tailored LIS is scarce. Three studies have reported worse fecal continence scores with the traditional LIS, whereas one study did not report any difference.(73-75) Irrespective of the LIS technique, incidence of fecal incontinence reduced from 10% before 2000s to 3.4% between 2000 and 2017.(50)

Male vs female: Lateral internal sphincterotomy (LIS) up to dentate line level is the treatment of choice in male patients with CAF, whereas in female patients LIS is not typically performed during the child-bearing age due to an increased risk of anal incontinence. However, there are reports of open LIS of about 20% of total left lateral internal sphincter length to be safe and effective in suitable female patients, with high success rates and without affecting anal continence.(76)

Repeat/re-do LIS: This has been reported to be performed for recurrent fissures in limited series only, and hence larger sample size and longer follow-up are needed to draw any definitive conclusions.(77, 78) Contralateral sphincterotomy has been also reported for recurrent fissures (78)

b. Fissurectomy

Fissurectomy involves excision of the fissure along with removing hypertrophied anal papilla, rolled out or indurated lateral edges, skin tags. Three randomized studies that compared Fissurectomy to LIS reported superior healing rates with the latterand equal incontinence rates with both.(79, 80)

In a meta-analysis, healing rate following anoplasty and/or fissurectomy was estimated to be 79.8%, and the incontinence rate was 4.9%.(63)

c. Anal dilatation

Over the years, anal dilatation fell into disrepute due to high recurrence of disease as well as the high incontinence rates. Potential for further future weakness of the sphincter due to age related changes, obstetric trauma, surgical interventions or radiation to the anal canal is to be also considered. Significant damage to the anal sphincter complex has also been noted on postdilatation procedural radiological evaluation.

Part of the problem is due to inability to standardize the procedure, because of individual variabilities such as (a) the force applied while stretching/dilating, (b) extent and duration of holding the stretch (c) anatomic variables in the anal canal musculature among patients (d) perceived anal tone/resistance after administration of anaesthesia. However, many surgeons still continue to discuss this practice. In recent years there have been attempts at standardizing the anal dilatation/stretch by endo-anal dilatation using calibrated dilators and pneumatic balloons, instead of the classical four finger stretch. Hence, we have revisited anal dilatation, analysed available data, and have framed recommendations accordingly.

Manual anal stretching: Dilatation of the anal canal using upto four fingers is termed as Manual Anal stretching. This technique has fallen into disrepute due to the high incidence of sphincter damage, postoperative incontinence, poor fissure healing rates, and recurrence

of disease. Present survey of literature shows inferior results of manual anal dilatation for the treatment of fissure in ano.(62, 67, 81-88) It is recommend that manual anal dilatation should not be performed. Literature survey yields good quality of evidence for the same.

Endoanal dilatation: This is controlled dilatation of the anal canal using a pneumatic balloon, self-retaining retractor or using calibrated dilators. Literature survey shows similar healing rates compared to internal sphincterotomy, but lesser incontinence rates when using endoanal balloon dilatation compared to internal sphincterotomy.(89, 90) Comparable results were also achieved while using endoanal balloon dilator and parks anal retractor.(91-99) Anal dilatation using calibrated dilators achieved poorer results compared to other modalities including self-finger massage of the area.(100)

Literature survey yields case series, retrospective and poorly structured studies. There were also no comparable standards for size of dilatation (varying diameters between 20 to 40 mm), pressure (1.4 atmospheres) to be used and the duration (varying between 60 to 360 seconds) of dilatator application. Although the use of these modalities appear to be safe, well-structured studies are required before advising routine use. There is also a need to standardize the diameter of dilatation, duration of application of dilatation and the pressure for dilatation. Several studies show inferior efficacy of anal dilatation compared to LIS in terms of healing rates and incontinence that was again confirmed in a Cochrane systematic review.(67, 84, 86-88)

d. Anal Advancement Flap

Anal Advancement Flaps (AAF) have also been utilized in the treatment of chronic anal fissure. The procedure typically involves a subcutaneous flap with an incision made from the anal verge extending caudally. The skin flap is then advanced into the anal canal and positioned to cover the anal fissure and sutured in place.

Anal Advancement Flap is proposed as a sphincter-preserving alternative to address anorectal seepage and to reduce the incontinence associated with LIS. It is recommended in the management of low pressure anal fissure. It involves transferring well-vascularized healthy tissue onto the fissure base using various flap techniques such as Y-V flap, rotation flap and V-Y island advancement flap. The AAFs' are associated with fissure healing rates between 80% to 100% with low rates of minor fecal incontinence (0%–6%).(77, 101-104)

Two independent studies showed a 98% success rate with advancement anoplasty for the treatment of chronic anal fissure, irrespective of anal tone.(105, 106) One prospective randomized trial of lateral internal sphincterotomy versus advancement flap found no significant difference in healing rates (100% in the sphincterotomy group vs. 85% in the flap group).(77) Incontinence was not observed in either group.

In a meta-analysis by Sahebally et al., AAF's showed significantly lower rate of anal incontinence compared to LIS (OR 0.06, 95% CI: 0.01–0.36, P = 0.002). Rate of unhealed fissure (OR 2.21, 95% CI: 0.25–19.33, P = 0.47) or wound complication rates (OR=1.41, 95% CI: 0.50–4.99, P = 0.51) were similar between AAF and LIS. However, larger, multi-center prospective comparative trials are required to further position anal advancement flap in the management of anal fissures.(107) Small non-comparative studies with anal flap combined with botulinum injection showed rapid symptom relief with healing rates ranging from 86.7% to 92% with lower fecal incontinence rates at follow-up period of up to 24 months.(108, 109) Similarly, anal flaps with LIS reported lesser postoperative pain, faster healing, fewer soiling episodes, low rates of recurrence and fecal incontinence.(104, 110) The addition of AAF to fissurectomy allows healthy well-vascularized skin in the ischemic area that promotes wound healing and reduces the risk of anal stricture.(111) Most studies evaluating fissurectomy with AAF for refractory anal fissures are small but have shown good healing rates with low incidence of incontinence and wound complications.(105, 112)

The advancement flap is an appropriate alternative to lateral internal sphincterotomy and may be particularly helpful in patients with low-pressure fissures.

Summary of studies from India

In a comparative randomized study by Vaithianathan et al., complete fissure healing at 6 weeks was observed in 71% patients treated with diltiazem, whereasit was achieved in 95% of patients who had undergone LIS.(39) In another randomized study, Giridhar et al. showed a healing rate of 88.5% in patients treated with diltiazem and 100% in those treated with LIS. The authors suggested topical diltiazem to be considered as first-line treatment in chronic fissure in ano with LIS being reserved for patients with relapse and therapeutic failure.(113) Some randomized studies also found closed LIS to be superior in terms of healing and recurrence rates compared to open LIS procedure.(68-70) Nikhat et al. showed tailored LIS as a safe and effective surgical procedure for CAF management with lower incontinence rate compared to the gold standard, LIS.(114) In a study by Paul et al., around 33.33% patients who were managed medically by 0.2% glyceryltrinitrate did not have relief of symptoms. Patients undergoing surgical management had more relief of symptoms (86.6%).(115) A study by Pandit et al., reported similar efficacy with dilatation and LIS, but higher rates of incontinence and recurrence with dilatation.(116)

ACRSI Recommendations on surgical management

- Lateral internal sphincterotomy is recommended as a second-line therapy following failure of first-line medical management. (Strong recommendation based on high-quality evidence, 1A)
- Lateral internal sphinceterotomy may be considered as first-line treatment in select patients suffering from severe pain and spasm, who are are expected to be non-compliant to medical management, and with low risk for incontinence. (Weak recommendation based on low- quality quality evidence, 2C)
- Open and closed techniques of LIS have similar efficacy. Therefore, either technique can be recommended for treatment of CAF. (Strong recommendation based on high-quality evidence, 1A)
- Tailored LIS (tailored to the length of the fissure) shows similar-to-worse healing rates with low rate of incontinence compared to conventional (LIS). (Weak recommendation based on moderate-quality evidence, 2B)
- Lateral internal sphincterotomy has higher healing rates and lower rate of recurrence and incontinence when compared to fissurectomy and anal dilatation. (Strong recommendation based on high-quality evidence, 1A)
- Anocutaneous flap may be recommended as a sphincter-preserving alternative to LIS as it has lower rates of incontinence but inferior healing rates. (Weak recommendation based on moderate-quality evidence, 2B)
- We do not recommend manual anal dilatation. (Strong recommendation based on moderate-quality evidence, 2B)

4. Special population

A. HIV-positive patients

It is necessary to distinguish idiopathic anal fissures from HIV-associated ulcers and sexually transmitted diseases that cause anogenital ulcers, which are broad-based and deep with generally lower sphincter tone.(117-119) HIV-related anorectal disease can manifest as ulcers or fissures in atypical locations, away from the midline. Patients often have painless or persistent “gnawing” pain and associated with poor sphincter tone. Biopsy, viral culture, debridement and intralesional steroid therapy are the mainstays of treatment.(120) Optimizing antiretroviral therapy can effectively ameliorate the symptoms over a longer interval. Poor healing is most closely associated with ulcers with a positive culture for HIV.(121) Appropriate antibiotics should be used to treat syphilis or other sexually transmitted diseases. Idiopathic anal ulcers constitute a diagnosis of exclusion after ruling out Herpes simplex virus (HSV), *Cytomegalovirus* (CMV), *Mycobacterium Avium Complex*, gonorrhea, chlamydia, syphilis, fungus and cancer by histopathological examination.(122).

Treatment remains similar to that of the HIV-negative populationwith initiation of first-line conservative therapy involving warm soaks, stool softeners and topical ointments. Anoreceptive intercourse is discouraged. Treatment of the infective systemic disease should be started concurrently. Surgical management should be limited to only drainage of abscess if any, and debridement of slough.

B. Anal fissures during pregnancy and after childbirth

One-third of women after childbirth complain of peri-anal symptoms.(10, 11, 13, 14, 123) Peri-anal diseases have been linked to difficult labour.(124-126) This corresponds well with the occurrence of diseases at the time of delivery. A birth weight of > 3800 gms and prolonged straining during the second stage of labour of > 20 minutes are independently associated with peri-anal diseases of pregnancy and puerperium. The fissure tends to be acute, but with low pressure anal tone, and should be managed by medical therapy and lifestyle modifications. Fissure in the presence of sphincter hypotonicity will not improve with sphincter relaxants or sphincterotomy. Treatment measures should be directed towards healing of the fissure.(127, 128) Persistent, chronic fissure in postpartum women can be managed with fissurectomy and advancement flap with good results.(128) In treating fissures with hypertonicity, no significant difference in healing rates were noted in patients who underwent advancement flaps versus sphincterotomy. Tissue healing can be aided by advancement flap without the need for a procedure to decrease anal tone

C. Crohn’s disease

Fissures in Crohn's patients are usually a manifestation of active inflammation and should be suspected if fissures are atypical in location or appearance, or multiple in number. Fissures in Crohn's disease tend to be deeper in nature and can be associatedwith fistulas, and abscess formation, which if left untreated can lead to significant sphincter deformity.

Treatment should be directed toward continence preservation with medical management of the underlying Crohn's disease.(129-133) Surgical interventions

can be considered in patients with abscesses, and those who are not responding to medical management. If surgical intervention is inevitable, every effort should be made to minimize wounds, minimize damage to the mucosa and to the external sphincter, and to perform a closed subcutaneous LIS. Fissurectomy might be considered only when the edges of the fissure are densely fibrotic and are unlikely to heal after sphincterotomy alone.(132, 134)

D. Anal fissure in children

Anal fissure is more common in children younger than 3 years than in older children.(135) The initial 2 weeks, conventional therapy for anal fissure is a warm SITZ bath, local application of analgesic ointments, stool softners and behavioural therapy. They provide temporary relief but have high recurrence rate. In a randomized study, PEG alone showed similar rate of improvement compared to polyethylene glycol and topical diltiazem combined.(136) Tropical application of 2% diltiazem is a most effective and safe treatment for anal fissure in children. Diltiazem is superior to 0.2% Glyceryl trinitrite and 10% Lidocaine and had fewer side effects. Hence, diltiazem can be used as a first line pharmacotherapy for anal fissure in children. (137)Surgery is rarely indicated. For an indolent fissure resistant to healing, fissurectomy and lateral sphincterotomy can be done.(138, 139) The surgical technique is the same as for adults.

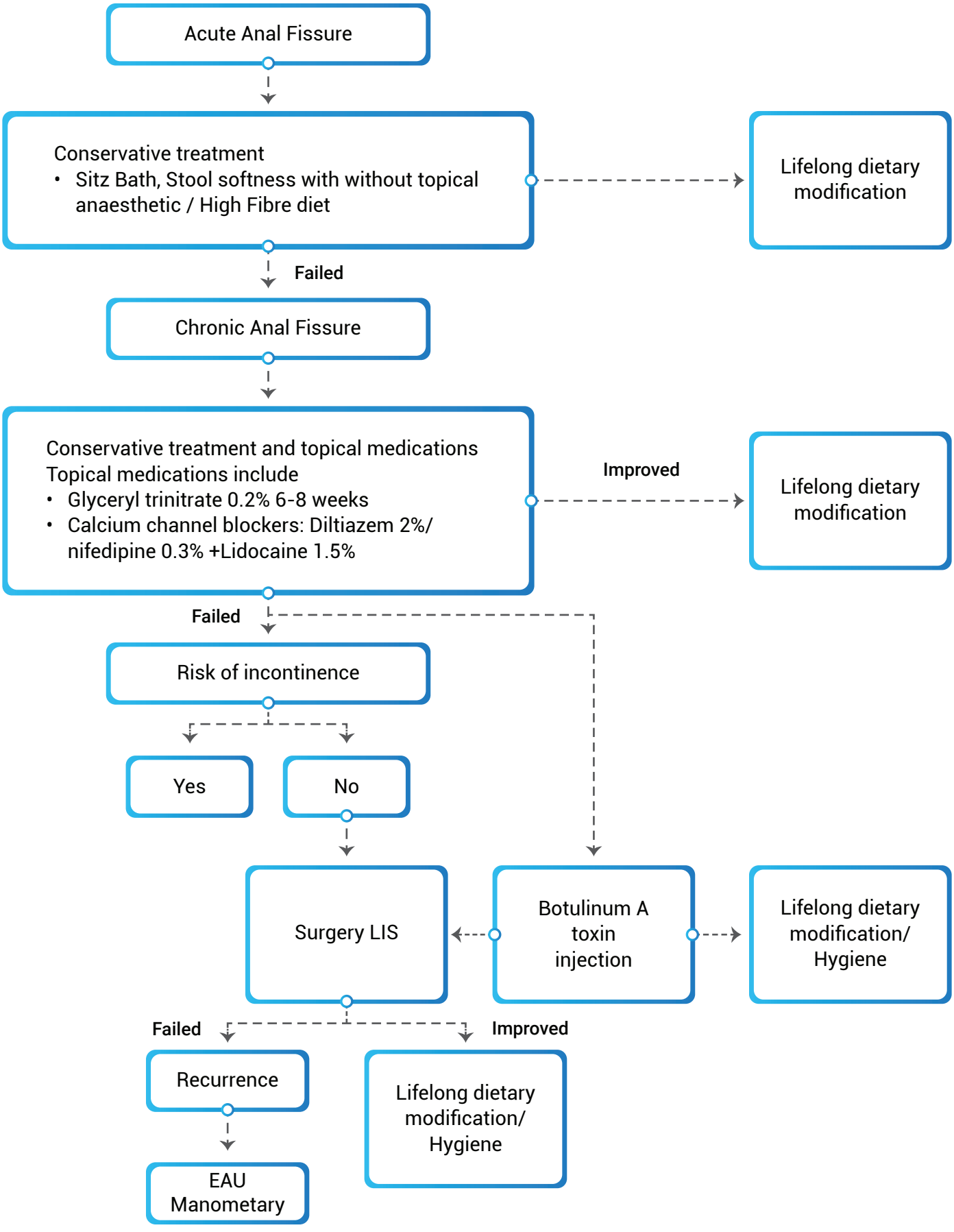
E. Anal tuberculosis

Extrapulmonary tuberculosis occurs in about 20% of patients with tuberculosis, (140) while abdominal tuberculosis constitutes about 10% of extra-pulmonary tuberculosis.(141) One percent of the digestive tract tuberculosis cases are anal tuberculosis and are difficult to diagnose.(140, 142, 143) The most common presentations of anal tuberculosis are as haemorrhoidal nodules, perianal abscess, or anal fistula and rarely fissure.(141) The different morphological forms of anal tuberculosis are ulcerative, verrucous, lupoid and miliary.(144, 145) The most common is the ulcerative form.(146-149) Tuberculous fissure-in ano is usually of ulcerative type.(150) Confirmation of diagnosis depends on histologic or bacteriologic analysis. The differential diagnosis includes: Crohn's disease, venereal lesions, neoplasia, foreign body reactions and sarcoidosis. According to our recent National Tuberculosis Elimination Program (NTEP) the recommended treatment regimen involves 6 months of treatment, the first two months with rifampicin, isoniazid (INH), pyrazinamide, and ethambutol, and the remaining four months with INH, rifampicin and ethambutol. The ulcerative lesions of the anus associated with tuberculosis regress in few weeks after starting the medical treatment of Tuberculosis. However, some patients need proloned treatment due to the poor response to anti tubercular therapy and tendency for recurrence. Surgical intervention may be required for obtaning tissue for histopathology, and if there is an associated persistent, discharging sinus/fistula or an abscess.(151)

ACRSI recommendationsons the managing fissures in special conditions

- Fissure in children should be treated initially by conservative measures. Failure of conservative measures should be an indication for medical management with local GTN or calcium channel blockers. Lateral sphincterotomy or fissurectomy should be reserved for those failing to heal with medical treatment (Strong recommendation based on low- and very-low-quality evidence, 1C).
- Fissure in ano secondary to anal tuberculosis, HIV or Crohn's disease should be managed medically, with concurrent treatment for the primary systemic disease. Surgical intervention should be limited to obtaining tissue for histopathological diagnosis and to drain any purulent collection. (Strong recommendation based on low quality evidence, 1C).
- Fissure in ano during pregnancy and after childbirth should be managed by conservative methods, as they tend to have low pressure sphincter tone. If the fissure persists and become chronic, surgical treatment by excision of the fissure with an anal advancement flap should be considered. (Weak recommendation with low quality evidence, 2C)

Algorithm


Acute Anal Fissure
Conservative treatment
• Sitz Bath, Stool softness with without topical anaesthetic / High Fibre diet
Lifelong dietary modification
Failed
Chronic Anal Fissure
Conservative treatment and topical medications
Topical medications include
• Glyceryl trinitrate 0.2% 6-8 weeks
• Calcium channel blockers: Diltiazem 2%/ nifedipine 0.3% +Lidocaine 1.5%
Improved
Lifelong dietary modification
Failed
Risk of incontinence
Yes
No
Surgery LIS
Botulinum A toxin injection
Lifelong dietary modification/ Hygiene
Failed
Improved
Recurrence
Lifelong dietary modification/ Hygiene
EAU Manometary

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***As compared to onset of action of stool softners like docusate. **Caution use in patients with impaired renal function. Currently no drug safety alerts on the Indian as well as worldwide health authority websites, Sep 2021. 1. Hannoodee S, Annamaraju P. Docusate. [Updated 2021 Jan 31]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2021 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK555942/ 2. Magnesium Hydroxide - Drugs.com [Internet]. Drugs.com. 2021 [cited 2 June 2021]. Available from: https://www.drugs.com/ppa/magnesium-hydroxide.html 3. Newton S, Hickey M and Brant J. Mosby's Oncology Nursing Advisor E-Book: A Comprehensive Guide to Clinical practice. 2nd edition. Elsevier publication; Pg no 290. 4. Sfetcu N. Health and drugs: Disease, prescription and medication. 2014 Laxatives 5. Susanne KH. et.al. Comparison of Bisacodyl and sodium picosulphate in the treatment of chronic constipation. Current Medical Research and Opinion. 2007;23(4):691-699 6. Patankar R. and Mishra A. A prospective non-comparative study to assess the effectiveness and safety of combination laxative therapy containing milk of magnesia, liquid paraffin and sodium picosulphate (Cremaffin-Plus*) in the management of constipation in patients with anal fissure/hemorrhoids/obstructive defecation syndrome. Int Surg J 2017;4:3899-906. 7. Portalatin M, Winstead N. Medical management of constipation. Clin Colon Rectal Surg 2012;25(1):12-19 8. Data on file. Liquid Paraffin, Milk of Magnesia & Sodium Picosulfate Oral emulsion, CREMAFFIN PLUS, COMPOSITION:** Each 5 ml (1 teaspoonful approx.) contains: Liquid Paraffin I.P. 1.25 ml ,Milk of Magnesia I.P.3.75 ml,Sodium Picosulfate B.P.3.33 mg ,Colours: Carmoisine & Ponceau 4R, **INDICATION:** For the symptomatic relief of constipation in adults. **DOSAGE AND ADMINISTRATION:** Adults and children over 12 years: 7.5 ml (approx. 1½ teaspoonful) if the response is unsatisfactory, the dose may be increased to 15 ml (3 teaspoonful) or as advised by the physician. Children 5 to 12 years .1 teaspoonful or as advised by the physician. Children 3 to 5 years,As advised by the physician. Children under 3 years. Not recommended Cremaffin Plus is best taken at bedtime preferably with water. Elderly: There is no need for dosage reduction in the elderly. **CONTRAINDICATIONS**: Patients with hypersensitivity to liquid paraffin, magnesium hydroxide or sodium picosulfate. Presence of intestinal obstruction, ileus, toxic megacolon gastric retention abdominal pain, nausea or vomiting, and in children under 3 years of age, patients with severely reduced renal function. **WARNINGS AND PRECAUTIONS:** In patients with renal impairment, Cardiac Arrhythmias, Colonic Mucosal Ulceration, Ischemic Colitis and Ulcerative Colitis, Use in Patients with Significant Gastrointestinal Disease. Prolonged use is not recommended. **PREGNANCY AND LACTATION:** The safety of Cremaffin Plus for use in pregnancy and lactation is not established. Therefore, as with other medicines, Cremaffin Plus should not be administered during pregnancy and lactation. **ADVERSE REACTIONS:** Liquid paraffin may cause anal seepage and irritation, granulomatous reactions. Nausea, headache, and vomiting are the most common adverse reactions (> 1%) reported with sodium Picosulfate and milk of magnesia. Abdominal pain, diarrhea, fecal incontinence, and proctalgia have been reported with sodium picosulfate. **OVERDOSAGE:** Gastric lavage may be performed where appropriate. Treatment should be symptomatic and supportive. **Issued on:** 5th Nov 2018 **Source:** Prepared based on full prescribing information version v3.0, dated: 29th Oct 2018 ®Trademark of the Abbott Group of Companies. For full prescribing information, please contact: Medical Sciences Division, Abbott India Limited, Floor 17, Godrej BKC, Plot No. C - 68, BKC, Near MCA Club, Bandra (E), Mumbai - 400 051.**

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