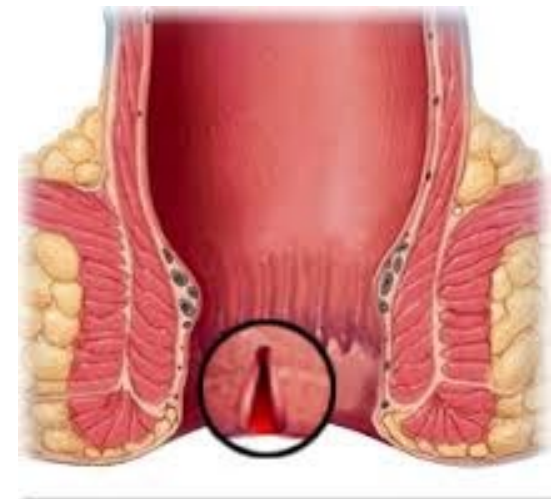


Anal Fissures: Medical and Surgical Management

WHAT ARE ANAL FISSURES ?

- A tear or ulcer in the squamous epithelium of the anus, usually in the posterior midline.
- Painful bowel movements that lasts hours after each bowel movement.
- Exact prevalence of anal fissures remains unknown.
- Many people avoid seeking treatment. Nevertheless, patients often end up seeking medical attention due to the combination of worrisome symptoms such as anal pain and bleeding.



Anal Fissure

EPIDEMIOLOGY

- Affect men and women, equally.
- Women are more predisposed to developing an anterior fissure as compared to men (25% vs. 8% respectively).
- 87% cases - age of 20–60 years.
- In India, the prevalence of anal fissures among other anorectal conditions was reported to be between 30–40%.
- A study in a tertiary care center in India reported that among the patients admitted for anorectal ailments, anal fissures accounted for 30.7% of study population

RISK FACTORS FOR HEMORRHOIDS

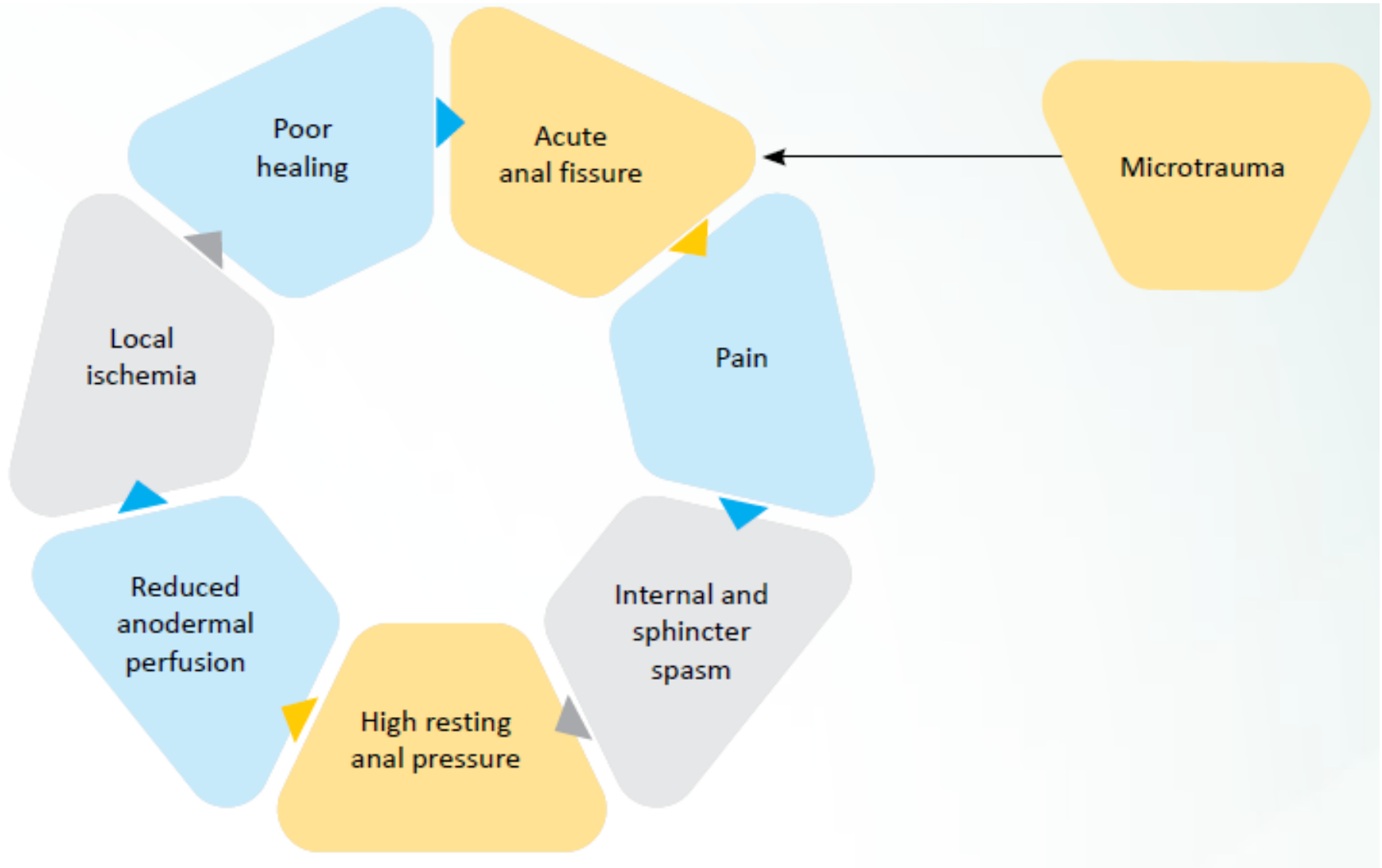
- **Primary fissures**

- Hard stools
- Prolonged diarrhea
- Vaginal delivery
- Repetitive injury
- Penetration

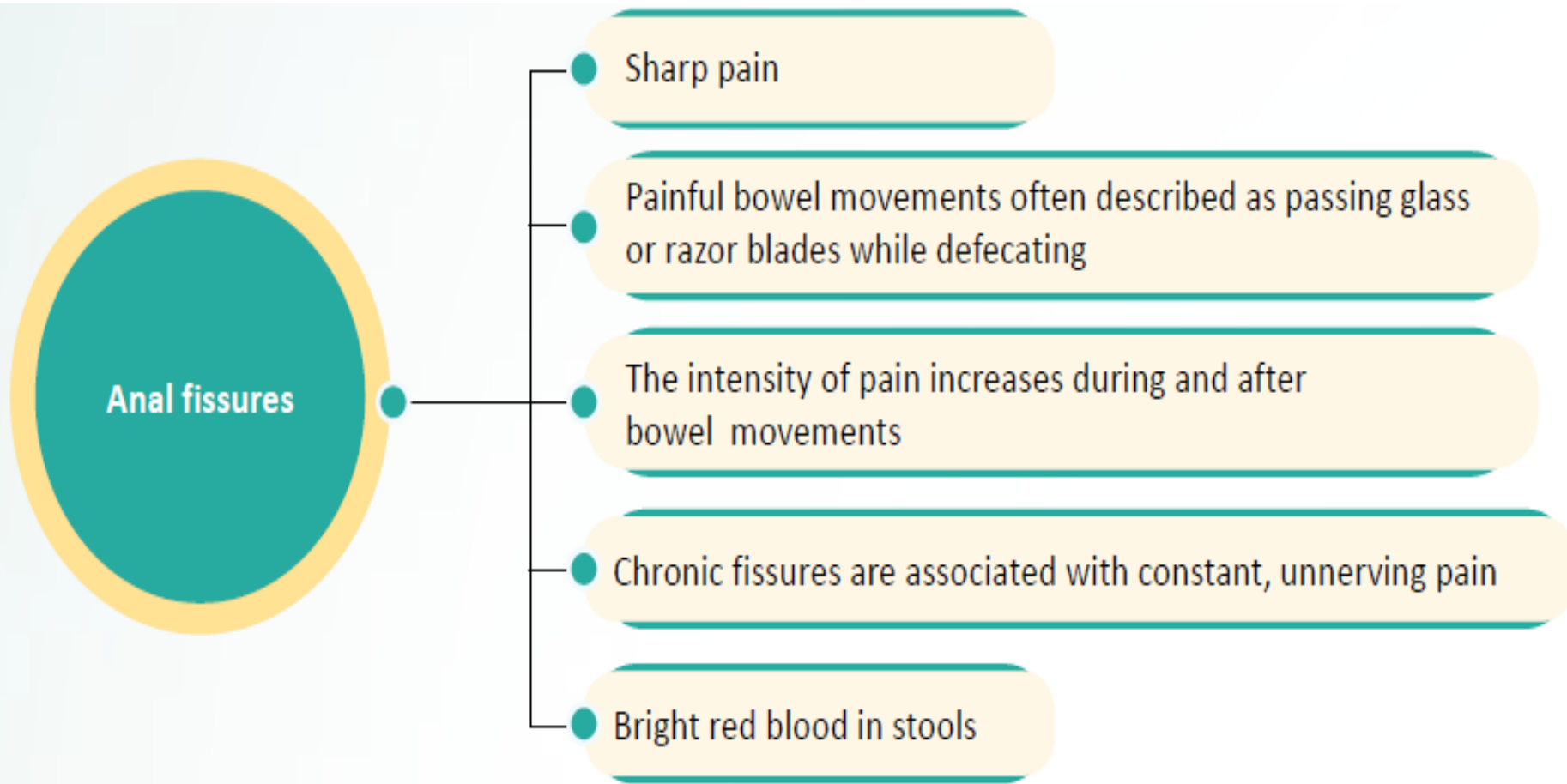
- **Secondary fissures**

- Previous anal surgical procedures
- Inflammatory bowel disease
- Granulomatous diseases
- Infections
- Malignancy

PATHOGENESIS



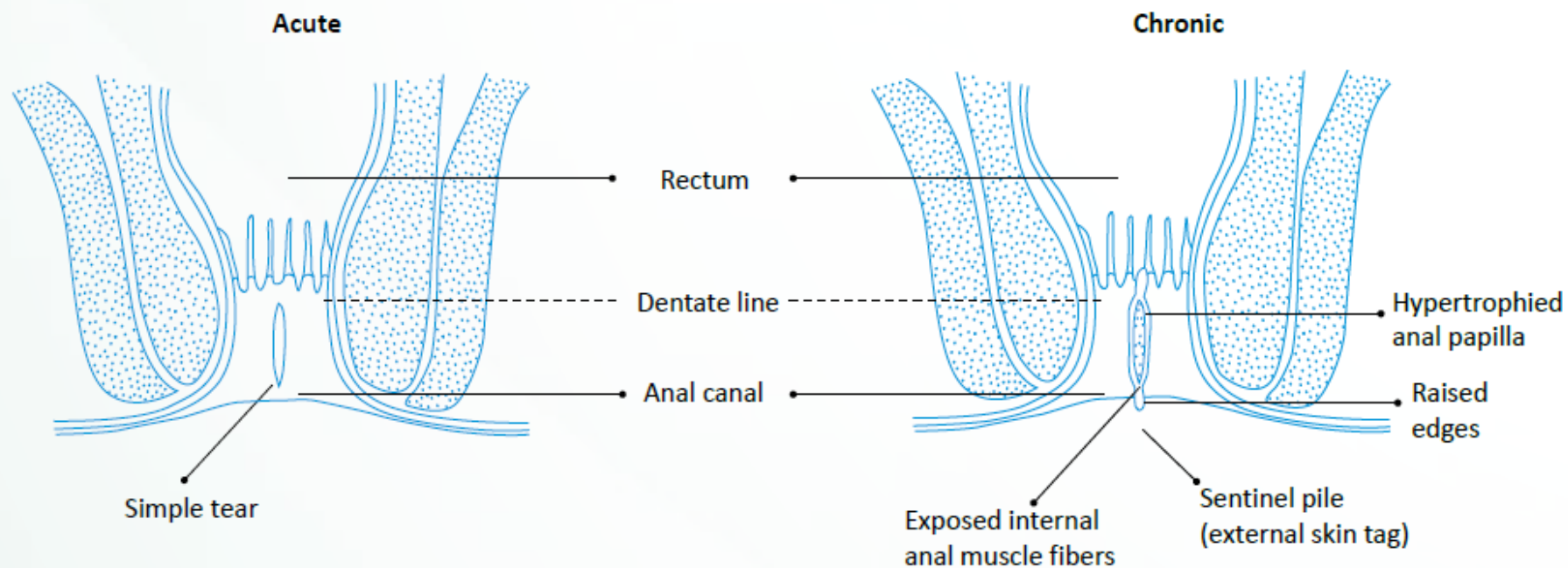
SIGNS AND SYMPTOMS



CLINICAL EXAMINATION

- Hypertonic sphincter shows some degree of tenderness
- Anal skin tags are common in patients with a more chronic fissure.
- May be difficult to perform digital rectal examination or anoscopy in the office due to the high level of pain
- Exposed fibers of internal anal sphincters at the base and hypertrophied anal papilla at the proximal extent.
- Edges of a chronic fissure may show edema, fibrosis or headed-up granulation.
- Approximately 90% of anal fissures in both men and women are located posteriorly in the midline while anterior fissures occur in some patients.

TYPES OF ANAL FISSURES



Management of Anal Fissures

CURRENT MANAGEMENT OF ANAL FISSURES

- The majority of acute anal fissures resolve without any significant intervention.
- Most of them resolve with a bowel management program including hot baths, psyllium fiber, a high-fiber diet, and increased intake of liquids.
- However, fissures that do not respond to these measures may be addressed using a variety of medical and surgical options

SURGICAL TREATMENT FOR ANAL FISSURES

Fissurectomy

- In fissurectomy, the surgeon resects the fissures with its lateral edges and removes poor quality tissues that heal poorly, substituting it with a clean wound that will heal.
- In posterior midline fissure, anoplasty may be used to resurface the defect, by advancing a rectal mucosal flap into the anal canal.
- Internal sphincterotomy in the bed of the fissure is especially useful in cases of anal fistula associated with infection.
- Complications associated with this technique are common in patients with keyhole deformity of the anal canal with fecal soiling.
- Fissurectomy and “chemical sphincterotomy” are combined to promote healing by resecting fibrosis and decreasing anal hypertonia while avoiding risks of incontinence.

Sphincterotomy

- Lateral internal sphincterotomy (LIS) remains the gold standard method for treating anal fissures.
- In LIS, the surgeon transects a portion of the internal anal sphincter, to relieve anal sphincter spasm with secondary ischemia and poor healing of the anoderm.
- Performing the closed technique results in a minimal incision that heals in a few days.
- Combination of sphincterotomy with debridement of the base and edges of the fissure results in a higher patient satisfaction.
- Performing the open technique seems to increase the risk of incontinence for flatus with no benefit for healing.
- Wound closure using the open approach, allows healing two times faster (15 days vs. 30 days) with less infection.
- In terms of healing and risk of recurrence, LIS is more effective than specific medical treatment, forcible dilatation and fissurectomy, albeit at the price of some risk of impaired continence.
- Bleeding, hematoma, local infection, and particularly anal incontinence are the reported complications of LIS.

Calibrated lateral internal sphincterotomy	<ul style="list-style-type: none"> Two techniques namely, a sphincterotomy extending to the apex of the anal fissure but not beyond the dentate line, and sphincterotomy calibrated dilatation to allow dilatation of the anal canal to a diameter of 3 cm, have been described in order to reduce the risk of post-sphincterotomy incontinence. A healing rate similar to LIS (90%) with less than 10% incidence of anal incontinence has been reported in studies.
Anoplasties	<ul style="list-style-type: none"> Anoplasties helps in resurfacing the floor of the debrided fissure with a flap of skin or rectal mucosa. Observational studies of anoplasties have demonstrated good results for healing without trouble of continence. Controlled trials comparing anoplasty to LIS have shown promising results. But there is not enough data to decide in their favor. Anoplasties are particularly useful in patients at high risk of anal incontinence after sphincterotomy since they have the advantage of not injuring the internal anal sphincter.
Anal dilatation	<ul style="list-style-type: none"> Anal dilatation reduces sphincter spasm by causing rupture of the internal sphincter. Uncontrolled anal dilatation is three times less effective than LIS with a 51% risk of permanent anal incontinence and is no longer recommended Emerging techniques in the recent years are based on the same principle but using a more controlled and standardized approach to anal dilatation In “Sphincterolysis”, firm finger pressure is used to rupture the internal sphincter fibers. This results in a healing rate of 96.5% with a 3.5% incidence of anal incontinence that recovers in 97% of cases.

MEDICAL TREATMENT FOR ANAL FISSURES

Topical nitrates

- Dilute NTG ointment is effective for the control of sphincter spasm-related pain and the healing of chronic anal fissure.
- Headache is the most common side effect occurring in 20–30% of cases and may require discontinuation of treatment.
- Headache can be prevented by oral analgesics and by gradually increasing the NTG dosage over four to five days.
- The healing rate is comparable with injection of botulinum toxin or topical application of CCB, but it is significantly less than after LIS or use of anal dilators.
- The rate of long-term recurrence ranges from 51–67%.
- The use of topical NTG has decreased the need for surgery in some practices

CCBs

- The two most studied CCBs are diltiazem and nifedipine, applied topically as a 2% ointment. Two applications per day for 6 to 8 weeks are prescribed.
- They have been reported in healing the anal fissure in 65–94.5% of cases.
- Common side effects include headache and pruritus ani in about 10% of cases.
- The safety and efficacy of topical CCBs is better than oral medication.
- The efficacy of CCBs is comparable to nitrates. However, CCBs are associated with fewer side effects as compared to NTG.

Botulinum toxin A

- Botulinum toxin inhibits presynaptic re-uptake of acetylcholine. Its injection causes sustained relaxation of the internal sphincter, treating both the painful sphincter spasm and the vascular component and promoting healing of the fissure.
- There is no data on the appropriate dose, the site or the number of injections; usually 30–50 units of botulinum toxin are injected into the internal anal sphincter in the posterior commissure on either side of the fissure.
- Botulinum toxin demonstrated a healing rate of 73%. The latest Cochrane meta-analysis demonstrated a similar efficacy to NTG.
- Botulinum toxin is less effective than lateral internal sphincterotomy, which has a 1.3 times greater chance of healing and a recurrence rate six times less frequent.
- However, sphincterotomy is associated with a nine times more common risk of anal incontinence for gas
- Overall, botulinum toxin results in an average healing rate of 67.5% with a recurrence rate of 50% at one year.

CCBs: Calcium channel blockers; NTG: Nitroglycerin; LIS: Lateral internal sphincterotomy.

GUIDELINE RECOMMENDATIONS FOR TREATMENT OF ANAL FISSURES – FOCUS ON TOPICAL CALCIUM CHANNEL BLOCKERS AS FIRST-LINE THERAPY

Guideline	Recommendation	Quality of evidence, grade
Clinical Practice Guideline ¹⁰	Compared with topical nitrates, the use of CCBs for chronic anal fissures has a similar efficacy, with a superior side effect profile, and can be used as first-line treatment	Strong recommendation based on high-quality evidence, 1A
ACG Clinical Guideline ¹¹	Gastroenterologists and other providers should treat chronic anal fissure with topical pharmacologic agents such as a CCBs or nitrates	Strong recommendation, moderate quality of evidence
The Management of Anal Fissure: ACPGBI Position Statement ¹²	Topical CCBs has similar efficacy to GTN but with fewer side effects and should be recommended as first-line treatment in the management of anal fissure.	Strong recommendation based on high-quality evidence, 1A
<i>ACG: American College of Gastroenterology; ACPGBI: The Association of Coloproctology of Great Britain and Ireland CCB: Calcium channel blockers; GTN: Glyceryl trinitrate.</i>		

10. American Society of Colon and rectal surgeons (ASCRS)

Dis Colon Rectum. 2017;60(1):7-14; Am J Gastroenterol. 2014 Aug;109(8):1141-57; (Quiz) 1058; Colorectal Dis. 2008;10 Suppl 3:8-29.

GAPS IN CURRENT TREATMENT

- Internal anal sphincterotomy lowers the resting anal pressure to heal anal fissures.
- However, the postoperative period is associated with complications such as surgical risks and late permanent incidence of incontinence
- Chemical sphincterotomy involves the use of different agents including botulinum toxin, glyceryl trinitrate, and calcium channel blockers, such as diltiazem and nifedipine.
- Headache reported in as many as 90% of patients using nitrates and orthostatic hypotension due to possible vasodilatation following systemic absorption limits their use

GAPS IN CURRENT TREATMENT

- CCBs, such as nifedipine, increases blood flow and tissue irrigation that promote wound healing.
- This is mediated by its smooth muscle relaxation and vasodilation.
- Factors that limit the use of topical nitrates were not encountered with CCBs making them an attractive alternative therapy.¹³

BENEFITS OF FIXED-DOSE COMBINATIONS

- Application of local anesthetics provide immediate relief of pain and itching.
- Amide local anesthetics, such as lidocaine hydrochloride (LDH) are advantageous over ester-type as they are associated with allergic reactions and skin sensitization.
- Accordingly, many studies have reported the safety of repeated anorectal administration of 5% lidocaine ointment.
- Subsequently, lidocaine has been commonly used in combination products with different.
- Combination products of nifedipine (0.3% w/w) and lidocaine (1.5% w/w) in form of ointment showed higher efficacy in treatment of anal fissure compared to a control topical ointment of lidocaine (1.5% w/w) and hydrocortisone acetate (1% w/w)

Nifedipine + Lidocaine

MECHANISM OF ACTION

- **Pharmacodynamic Properties**

- Nifedipine, a dihydropyridine CCB, has a relaxing effect on the smooth muscles of anal sphincter, when used locally.
- It acts by reducing the hypertonia of the internal anal sphincter muscle.
- The action of nifedipine is complemented by the presence of lidocaine, a local anesthetic to relieve pain (blocks sodium channels and signal generation in peripheral nerve endings)

- **Pharmacokinetic Properties**

- The pharmacokinetic properties of nifedipine and lidocaine cream have been studied in healthy volunteers.
- The determination of the active ingredients in blood was negative.

CONTRAINDICATIONS

- Hypersensitivity to the active ingredient and in particular to lidocaine and other anesthetics of similar type/structure or any of the excipients.
- Pregnancy, ascertained or presumed and lactation

ADVERSE EFFECTS

- Local reactions such as pain, burning, itching, hyperemia and bleeding may occur.
- These effects resolve after discontinuation of treatment
- Local application of preparation with a basis of lidocaine causes an allergic reaction in very rare cases.
- During the phase of clinical trials, nifedipine and lidocaine did not show any side effects due to possible systemic absorption of the two active ingredient

WARNING AND PRECAUTIONS

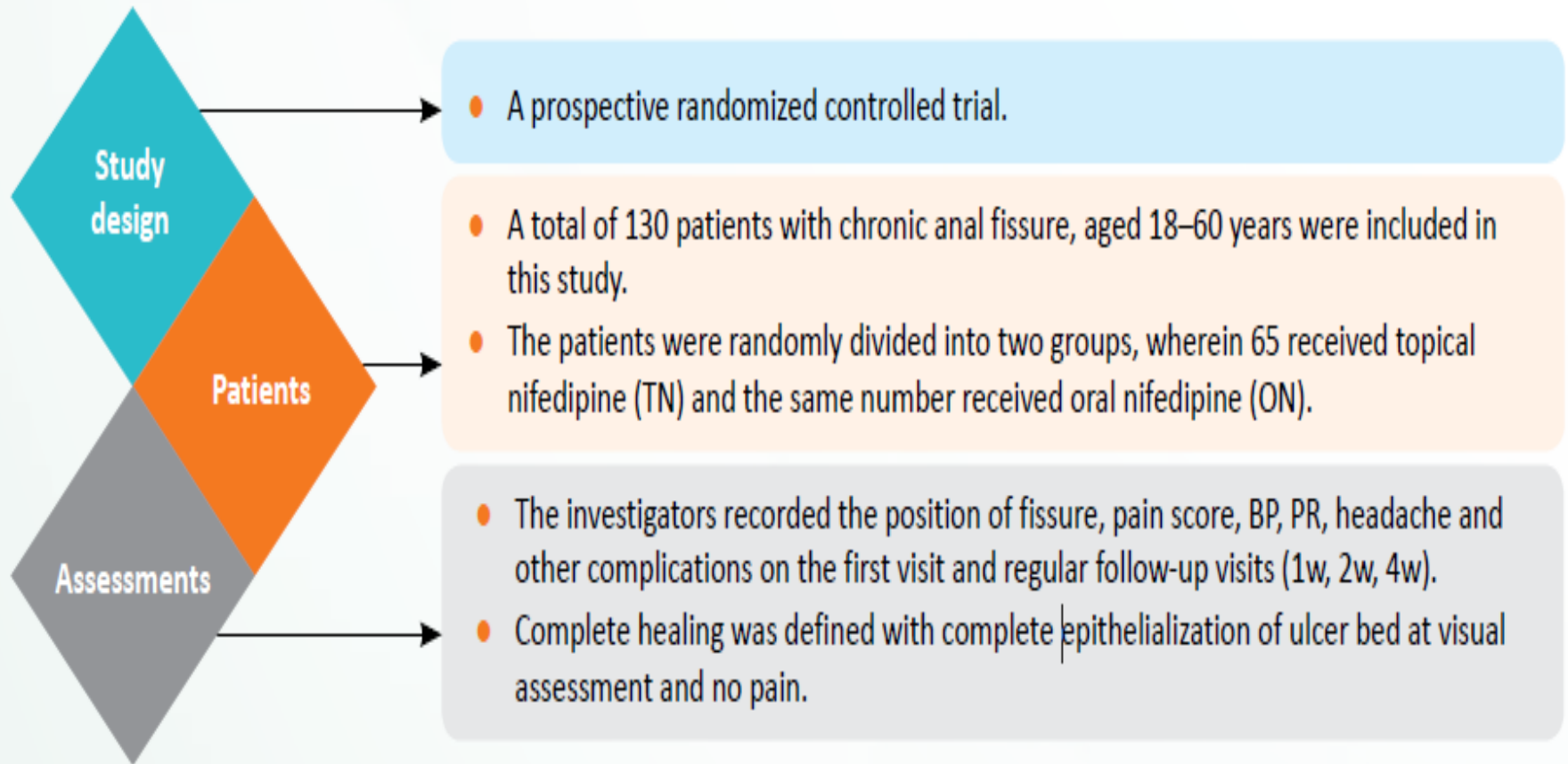
- Excessive topical application of the medicine for prolonged periods of time can give rise to phenomena of sensitization and reactions of local hyperemia, and bleeding that disappear with discontinuation of treatment.
- Extreme caution must be exercised while using nifedipine and lidocaine cream in patients with severely damaged mucosa and inflammation in the region to be treated, because, in such situations, there may be an excessive absorption of active ingredients.

WARNING AND PRECAUTIONS

- Nifedipine and lidocaine cream should be used under the supervision of a physician in very elderly patients as well as those under the age of 18 years and in patients treated with beta-blockers and anti-hypertensives.
- It is advisable in such cases to check blood pressure at the beginning and periodically during treatment.

Clinical evidence

ORAL VS. TOPICAL NIFEDIPINE FOR TREATMENT OF ANAL FISSURE



ORAL VS. TOPICAL NIFEDIPINE FOR TREATMENT OF ANAL FISSURE

- The final number of patients in the topical nifedipine (TN) group was 60, and in the oral nifedipine (ON) group was 59
- The rate of ulcer healing in the TN group was significantly better compared to the ON group (73.33% vs. 49.5% respectively, $p < 0.05$)
- ON group had more prevalent side effects such as headache and flushing than TN group, which was statistically different.
- The VAS score was comparable in both the groups.

NIFEDIPINE GEL PLUS LIDOCAINE FOR THE TREATMENT OF ANAL FISSURE

Patients

- A retrospective review of 106 children with acute anal fissure undergoing treatment during a 10-year period.
- Inclusion criteria comprised of finding a typical acute deep anal fissure and children between 0–17 years of age.

Intervention

- Patients were treated with nifedipine 0.2% and lidocaine 5% ointment two or three times a day for 4 weeks, based on the severity of symptoms and physical finding.

Assessment

- All patients were clinically evaluated for complete healing of the fissure after one month of continuous treatment.
- In cases of improvement but not complete healing, the same treatment protocol was followed for a second month, and the patient were reevaluated
- Recurrence was only considered for those patients presenting with similar symptoms and physical findings months or years after complete healing of the fissure.

NIFEDIPINE GEL PLUS LIDOCAINE FOR THE TREATMENT OF ANAL FISSURE

- 93.40% patients achieved complete healing of the fissure after completion of 4-week treatment course
- Symptoms recurred in a total of 7 patients who required a second 4-week treatment in 2, 4, 11, 18, 19 and 24 months (2 patients), respectively.
- The observed recurrence rate was very low (6.6%)
- The mean follow-up was 3.67 years, ranging from 6 months to 9 years.
- No side effects of nifedipine were observed.

EFFICACY AND SAFETY OF NIFEDIPINE AND ISOSORBIDE DINITRATE IN CHRONIC ANAL FISSURE

Study design

- A double-blind clinical trial study performed in 2012–2013

Patients

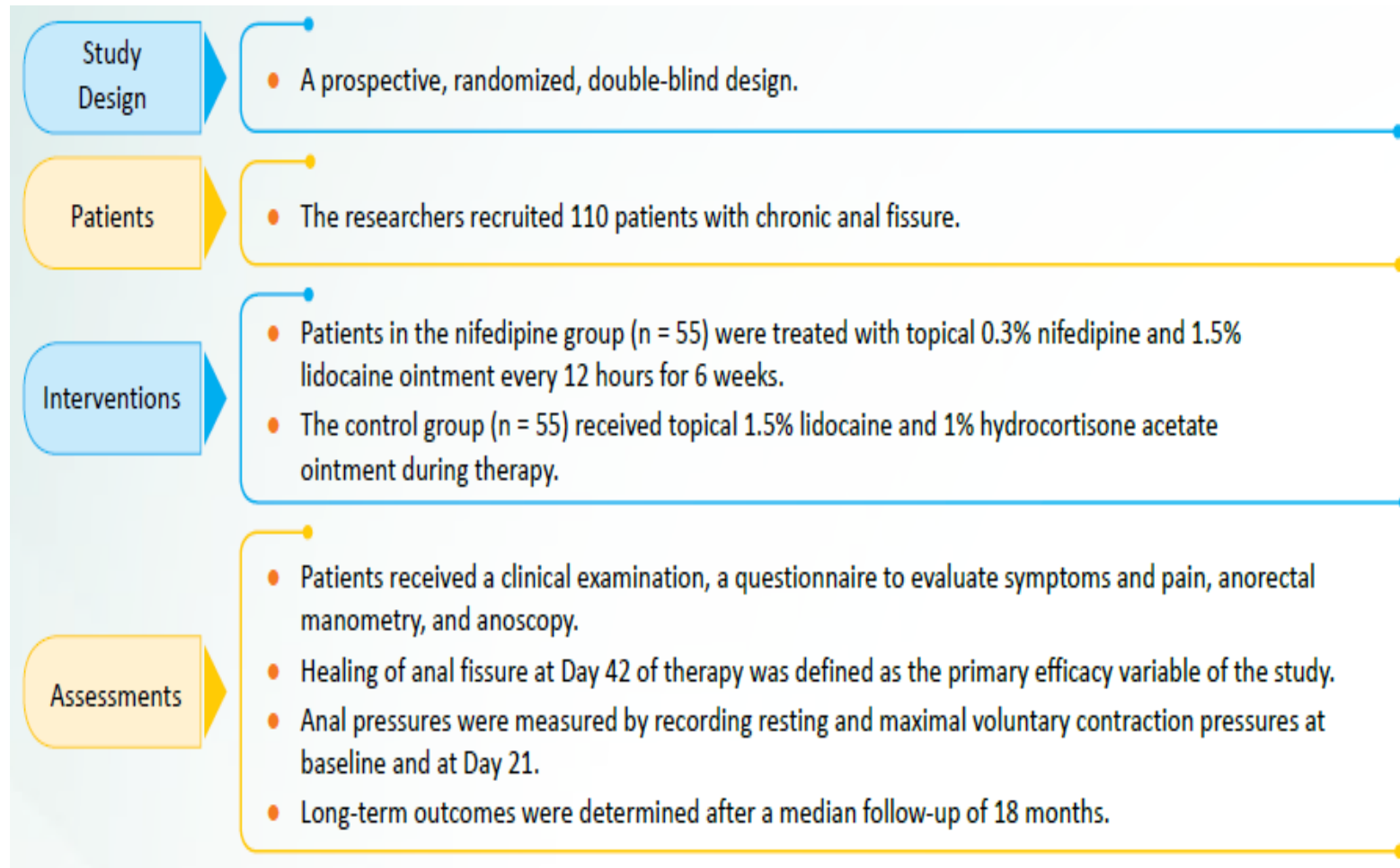
- Patients aged 20–60-years-old, with a primary diagnosis of chronic anal fissure were included
- The patients were randomized into two groups: nifedipine 0.3% (n = 35) or isosorbide dinitrate 0.2% (n = 35) applied three times a day for three weeks.

Assessments

- The researchers examined patients on the 7th, 14th, and 21st days of treatment, and assessed the symptoms including bleeding, pain, and healing status, as well as the side effects of the drugs.
- Pain was evaluated using a visual analogue scale (VAS).

- On Day 21, the mean VAS in the ISDN group was 0.91 (SD 0.01) and in the nifedipine group was 0.45 ± 0.78 , with a statistically significant difference ($p = 0.038$)
- The bleeding was similar in the two groups ($p = 0.498$).

TOPICAL NIFEDIPINE WITH LIDOCAINE OINTMENT VS. ACTIVE CONTROL FOR TREATMENT OF CHRONIC ANAL FISSURE



TOPICAL NIFEDIPINE WITH LIDOCAINE OINTMENT VS. ACTIVE CONTROL FOR TREATMENT OF CHRONIC ANAL FISSURE

- A total of 94.5% of nifedipine treated patients achieved healing of chronic anal fissure ($p < 0.001$) as opposed to 16.4% of the controls
- In the nifedipine group, the mean anal resting pressure decreased from a mean value \pm SD of 47.2 ± 14.6 to 42 ± 12.4 mmHg.
- This represents a mean reduction of 11% ($p = 0.002$).
- The nifedipine group was not associated with any systemic side effect.
- After removal of the blinding, within 1 year of treatment, recurrence of the fissure was observed in 3 of 52 patients in the nifedipine, and 2 of these patients healed with an additional course of topical nifedipine and lidocaine ointment.

TOPICAL NIFEDIPINE VS. TOPICAL GLYCERYL TRINITRATE FOR TREATMENT OF CHRONIC ANAL FISSURE

Study Design

- A prospective, double-blind trial.

Patients

- A total of 52 patients suffering from chronic anal fissure were randomly and equally allocated to receive either glyceryl trinitrate or nifedipine, both applied topically to the perianal region.

Endpoint

- The end point of the study was healing within a predetermined period (6 months).

Assessments

- Variables assessed included demographic data (age, gender), symptoms associated with the fissure, duration of treatment, percentage of healing, untoward effects of treatment, pain scores, duration of follow-up, recurrence, and need for complementary means of treatment.

TOPICAL NIFEDIPINE VS. TOPICAL GLYCERYL TRINITRATE FOR TREATMENT OF CHRONIC ANAL FISSURE

- Nifedipine group had a higher healing rate (89%; $p < 0.04$) with as compared with GTN (58%).
- GTN group was associated with higher rate of treatment side effects (headache, flushing) as compared to nifedipine (40% vs. 5% respectively; $p < 0.01$).
- Both groups had significantly lower pain scores ($p < 0.03$) on completion of treatment (3.2 from 6.2 in GTN, and 3.4 from 6.1 in nifedipine), but did not differ between the two groups.
- Recurrence occurred in 31% of patients treated with GTN after a mean period of 18 ± 3 weeks and 42% of those treated with nifedipine and after a mean period of 12 ± 4 weeks, respectively.

CONCLUSION

- **Anal fissure represents one of the most common anorectal problems.**
- **Among all the anorectal conditions encountered in India the prevalence of anal fissures has been reported to be between 30–40%.**
- **Acute injury to the internal sphincter results in local pain and spasm, a high resting pressure, reduced blood flow and ischemia which subsequently delays the wound healing process.**
- **The inclination of fissures towards the posterior midline section may be attributed to the poor perfusion of this portion.**
- **The diagnosis of an anal fissure is confirmed by history and physical examination without the need to carry out further investigations.**

CONCLUSION

- **Postoperative period associated with complications, such as surgical risks and late permanent incidence of incontinence, warrants for alternative regimens for the treatment of anal fissures.**
- **Unlike CCBs, nitrates were not associated with systemic side effects that limited their use, making them an attractive alternative therapy.**
- **Combination products of nifedipine and lidocaine in form of ointment shows a good efficacy in treatment of anal fissures.**
- **Although oral nifedipine can reduce symptom and signs of anal fissure, topical nifedipine has a superior role for anal fissure treatment with higher healing rate and lower side effects.**
- **The results of the study demonstrated that the therapeutic use of nifedipine should be extended with local use to the conservative treatment of anal fissures.**
- **Topical 0.2% nifedipine with lidocaine appears an efficient mode of treatment for anal fissures in children, with a significant healing rate and no side effects.**

CONCLUSION

- **In view of the findings on healing status and pain in the patients, nifedipine may be significantly more effective in the treatment of chronic anal fissure than ISDN.**
- **5% nifedipine ointment, used as an agent in chemical sphincterotomy, appears to offer a significant healing rate for acute anal fissure and might prevent its evolution to chronicity.**
- **The results of the study demonstrated that the therapeutic use of topical nifedipine and lidocaine ointment should be extended to the conservative treatment of chronic anal fissure.**
- **Nifedipine ointment showed better results than GTN ointment in chronic anal fissure regarding headache, compliance, healing and recurrence in 6 weeks of follow up period after complete healing of fissure in 8 weeks.**
- **Topical application of nifedipine for management of chronic anal fissure was more effective and had fewer side effects than topical GTN. Recurrence was frequent with both drugs.**

Thank you