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A Comparative Study in Treatment of Anal Fissure – Topical Diltiazem vs Topical Nitroglycerin

Rommel Singh[1], Reetinder Kaur Chahal[2]*, Kuldip Singh[3], Gagandeep[4]

[1]Associate Professor, Govt. Medical College and Rajindra Hospital, Patiala, Punjab, India. Email: rommelmohi@gmail.com, Orcid: 0000-0003-1230-4151.
[2]Assistant Professor, Govt. Medical College and Rajindra Hospital, Patiala, Punjab, India. Email:reetinderchahal@gmail.com, Orcid: 0000-0002-4972-9260
[3]Professor, Govt. Medical College and Rajindra Hospital, Patiala, Punjab, India.
Email: kuldips3@gmail.com, Orcid: 0000-0002-0875-0450
[4]Junior Resident, Govt. Medical College and Rajindra Hospital, Patiala, Punjab, India.
Email:drgagandeep89@gmail.com, Orcid: 0000-0002-1231-0423

*Corresponding author

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Abstract

Background: Anal fissure is a common condition in surgical practice. The present study was conducted in the Department of General Surgery, Govt. Medical College, Patiala in 60 patients with diagnosis of anal fissure on outdoor basis. The treatment was done with topical application of 2% Diltiazem ointment and topical 0.2% Nitroglycerine ointment in 30 patients respectively. Patients were followed up for three months in OPD. The two groups were compared for degree of symptom relief, healing, any adverse drug effect and reccurence if any and analysed statistically. **Methods**: 60 cases were studied. The study population was divided into two groups of 30 patients each.Group A: This group of patients were be treated with topical application of 2% diltiazem per rectally twice daily for a period of 6 weeks with sitz bath and Oral antibiotics .Group B: This group patients were treated with topical application of 0.2% nitroglycerin/ Glyceryl trinitrate application over the anal verge twice daily for a period of 6 weeks along with sitz bath and Oral antibiotics. **Results:** On completion of therapy at 6 weeks healing was observed in 26(86.6%) patients in group A and in 21(70%) patients in group B, so there was no statistically significant difference between diltiazem and nitroglycerin group in healing of anal fissure at 6 weeks therapy. At 6 weeks follow up headache occurred in 15 patients, out of which 1 was in group A and 14 were in group B. Itching occurred in 4 patients, Out of which 3 were in group A and one was in group B. So there was no statistically significant difference between Diltiazem and Nitroglycerin group in adverse effect profiling except headache which came out as statistically significant in group B. **Conclusions:** Chemical sphincterotomy with topical 2 % Diltiazem gel is an effective first-line treatment for anal fissures, achieving symptom relieving and healing rates comparable to those achieved with 0.2 % Nitroglycerin ointment but with relatively few, generally acceptable side effects as compared to distressing adverse effects of nitroglycerin as headache.

Keywords:- Anal Sphincter tone,Chronic anal fissure, External Anal Sphincter, Nitroglycerin, Internal Anal Sphincter, Nitric oxide.

INTRODUCTION

Fissure-in-ano is defined as a longitudinal split in the anoderm of the distal anal canal which extends from the anal verge proximally towards, but not beyond, the dentate line.[1] Anal fissure or fissure-in-ano is a common condition in surgical outpatient door. It can be

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a very troubling and distressing problem because the severity of pain and discomfort disproportionate to the severity of physical lesion. It may be too severe that patient may avoid defecation.[2] In 90% of cases, it occurs in the posterior midline.[3] Site is also peculiar, in males it is seen in mid posterior aspect while in females it is also seen in mid anterior and lateral aspect.[4] The pathogenesis of anal fissure is poorly understood. Most anal fissures are idiopathic with no underlying disease process [Lund and Scholefield et al., 1996] and there is no simple and unified theory to explain their genesis.[5] The principle aim of the treatment of chronic anal fissures is to decrease internal sphincter tone and hence increase the blood flow for tissue healing. Treatment include pharmacological and surgical modalities. Anal fissure usually does not heal by simple conservative measures. They are most commonly treated surgically by four finger dilatation or lateral internal sphincterotomy under general or spinal anesthesia. Sphincterotomy results in a sustained reduction of maximum resting anal pressure.[6] But The internal sphincterotomy carries a significant rates of fecal or flatus incontinence, fecal urgency and soiling of perianal area.[7] Because of the possible pathogenesis that spasm of the internal sphincter and reduced blood flow to the sphincter play important role in formation and chronicity of anal fissure, Chemical sphincterotomy has been tried by using a variety of agents which include topical glyceryl trinitrate, calcium channel blockers such as nifedipine or diltiazem which can interrupt pathogenesis. In this study an attempt was made to study the comparison between topical diltiazem and topical nitroglycerin in treatment of fissure-in- ano.

Aims and Objectives

The present study is be carried out with the aim of comparing the efficacy and adverse effects of topical application of 2% diltiazem with 0.2% nitroglycerin in treatment of anal fissure with respect to following:-

Parameters; Symptom relief, Healin, Adverse drug effects, Recurrence.

MATERIAL AND METHODS

This Study was a prospective comparative study done in Rajindra Hospital Patiala. The Study Population was divided into two groups. 60 cases were studied. The study population was divided into two groups of 30 patients each.

Group A: This group of patients were be treated with topical application of 2% diltiazem per rectally twice daily for a period of 6 weeks with sitz bath and Oral antibiotics

Group B: This group patients were treated with topical application of 0.2% nitroglycerin/ Glyceryl trinitrate application over the anal verge twice daily for a period of 6 weeks along with sitz bath and Oral antibiotics.

Patients in each group were advised to consume fibre rich and high-water-content diet. In this study patients were treated on OPD basis. Patients were advised to apply 3 gram of ointment per 18 dose circumferentially 1 cm inside the anus, near the internal anal sphincter, every 12 hours for 12 weeks. Follow up is done by means of regular OPD visits at 2 weeks, 6 weeks and 3 months. Data analysis was conducted with Statistical chi squared and correlation tested. A value of $P< 0.05$ was considered significant..The study has been

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approved by the research ethics committee of GMC, Patiala and has been performed in accordance with the ethical standards.

Eligibility Criteria

1) Patients aged between ≥ 18yrs and ≤ 65 years;
2) Presence of anal fissure that had failed to resolve with simple measures such as laxatives & high fiber diet
3) Patients giving informed consent.

Exclusion Criteria

1) Patients who had previous surgery for anal fissure
2) Patients who require anal surgery for any concurrent disease like hemorrhoids,
3) Pregnant women
4) Patients with significant cardiovascular condition will be excluded from present study.
5) Patients with fissures secondary to other diseases like Crohns disease,ulcerative colitis, tuberculosis, anal warts, malignancy and sexually transmitted diseases.

Materials Used for Syudy:

- Diltiazem gel 2%
- Nitroglycerin ointment 0.2%

RESULTS

The following observations were recorded

Group A: Diltiazem gel treated group.

Group B: Nitroglycerin ointment treated group.

Age Incidence: The majority of patients were in the age group 19-48 (93.33%). The maximum number of patients being in the 19-28 years age group. The mean age is 35 years. Patients in age group 19-38 years are 40(66.67%) patients,39-48 years are 15(25%), and above 49 years are 5 (8.3%). On comparison,p value is 0.611 which is non significant statistically, so both groups were comparable for study.

Gender incidence: The majority of patients in the study were males 34(56.6%) and the females constituted 26(43.3%). In diltiazem group females were 12(40%) and males were 18(60%). In nitroglycerin group females were 14(46.67%) and males were 16(53.33%). On comparison, p value is 0.232 which is non significant statistically, so both groups were comparable for study.

Occupation: The incidence of anal fissure was found to be more in office workers, students and house wives. On comparison, p value is 0.587 which is non significant statistically, so both groups were comparable for study.

Presenting complaints:

Pain- All the 60 (100%) patients presented in the OPD with complaint of pain.Duration of pain was from 3-6 weeks in 39 (65%) patients. In 21 (35%)patients the duration of pain was from 1-2 weeks.

Bleeding- Complaint of bleeding was in 44 (73.33%) patients, out of which 18(60%) in diltiazem group and 26(86.67%) in nitroglycerin group

Constipation- Constipation was present in 36(60%) patients. Out of which 17 (56.67%) were present in diltiazem group and 19(63.33%) in nitroglycerin group.

Pruritis- Pruritus was present in 26 (43.33) patients, out of which 20 (66.67%) were in

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diltiazem group and 6(20%) were in nitroglycerin group

Local examination:

On local examination Position of fissure was mostly at posterior site in 52 (86.66%) patients, out of which 25 (83.33%) were present in diltiazem group and 27(90%) were present in nitroglycerin group. Anterior anal fissure was present in 5(8.33%) patients, out of which 3(10%) were in diltiazem group and 2(6.67%) were present in nitroglycerin group.Lateral anal fissure was present in 3 (5%) patients, out of which 2 (6.67%) were in diltiazem group and 1 (3.33%) was in nitroglycerin group. Thus posterior anal fissure were the commonest, anterior and lateral were least common. sentinel pile was present in 33(55%) patients in both groups, out of which 14 (46.67%) were in group A and 19(63.33%) were in group B. On local examination induration of some degree was present at the edges of anal fissure in total 37(61.66%) patients, out of which 16(53.33%) were in group A and 21(70%) were in group B .

Type- Out of total 60 patients 22 (36.66%) were of acute anal fissure and 38(63.33%) were of chronic anal fissure.

Follow up of patients– For pain - At 2 weeks pain was relieved in 28 (46.66%) patients, out of which 14 (46.66%) were in group A and 14(46.67) were in group B. So there was no statistically significant difference between diltiazem and nitroglycerin group in pain relief at 2 weeks.Also there was no statistically significant difference between diltiazem and nitroglycerin group in pain relief at 6 weeks.

Bleeding- At 2 weeks bleeding was relieved in 26(43.33%) patients, out of which 11 (36.67) were present in group A and 15 (50%) were present in group B, so there was no statistically significant difference between diltiazem and nitroglycerin group in relief of bleeding at 2 weeks. At 6 weeks bleeding was relieved in 41(68.33%) patients, out of which 16 (53.33%) were present in group A and 25 (83.33%) were present in group B, so there was no statistically significant difference between diltiazem and nitroglycerin group in relief of bleeding at 6 weeks.

Healing- On completion of therapy at 6 weeks there was no statistically significant difference between diltiazem and nitroglycerin group in healing of anal fissure at 6 weeks therapy as healing was observed in 26(86.6%) patients in group A and in 21(70%) patients in group B.

Follow Up of Adverse Effects- At 2 weeks follow up there was no statistically significant difference between diltiazem and nitroglycerin group in adverse effect profiling except headache which came out as statistically significant in group B with presence of headache in 12 patients in group B. At 6 weeks follow up headache occurred in 15 patients, out of which 1 was in group A and 14 were in group B, which is a statistically significant difference between Diltiazem and Nitroglycerin group in adverse effect profiling. Recurrence- Follow up 3 months showed recurrence in 5 (8.33%) patients, out of which 2 (6.67%) were in group A and 3 (10%) were in group B. So there was no statistically significant difference in recurrence of anal fissure in both the groups.

DISCUSSION

Resolution of symptoms of anal fissure and healing can be attained by invasive

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interventions or by chemical sphincterotomy. Because of the complications associated with operative lateral internal sphincterotomy and the risk of incontinence, medical alternatives of surgery have thus been tried to obtain. Chemical sphincterotomy is non invasive, precludes the need for general anaesthesia, and could be applied at home by the patient itself. A first line use of medical therapy cures most chronic anal fissures economically and conveniently. Diltiazem remains the standard chemical sphincterotomy against which other treatments are compared. Most of fissure were found in age group between age 19-38 years, that is 63.3% and mean age in our study was 34.5 years. Mean age that was reported in different studies ranges form 30-45 years which is almost same in our study. In our study mean age is 35.3 in group A and 34 in group B. Similar results were observed in study conducted by Muhammad Siddique et al 2017 with average age being 43 years and by Venkatesh S et al 2019, in which average age was 38 years.[8,9]

In our study, there was male preponderance in occurrence of anal fissure, showing 43.3% in females and 56.6% in males. The lower number of female (43.3%) patients in this study and other studies illustrated below may be due to the conservative attitude of females, especially for perianal diseases. These observations were compared with the studies conducted by m.siddique khan et al 2017,[8] in which 66.3% were male and 33.7% were female patients and Venkatesh et al 2019 showing 51% of male patients and 49% female patients.[9]

The pain associated with chronic anal fissures is usually marked, and together with bleeding and irritation, it causes considerable morbidity and reduction in quality of life in these patients. Patients of anal fissure presents mostly with chief complaints of pain, bleeding and pruritus ani. The common symptoms in our study were anal pain during and after defecation (100% patients), bleeding in 73.3% patients. These observations were compared with the studies conducted by Venkatesh et al 2019 showing bleeding in 82% of patients and in study conducted by Kevin M. Bonney showed bleeding In76% patients.[9,10]

In our study in 86.6% of patients fissures were present posteriorly, only 8.3% of patients had anterior fissure and 5% patients had laterally lying anal fissure. These observations were compared with the studies conducted by Venkatesh et al showing 83% posteriorly lying anal fissure.[9]

In the present study a comparative evaluation of DTZ gel (2%) and GTN ointment (0.2%) was performed to assess the effectiveness in terms of pain relieve and healing and adverse effects of these two pharmacotherapies in the management of anal fissure. The results were comparable to studies conducted by Shahram ala et al 2012 and Behnam sanei et al 2009.[11,12] In our study, healing of anal fissure at the end of 6 weeks, in group A was 86.6% and in group B was 70%, which was statistically insignificant. These results were comparable to studies done by Ansari et al,[13] and Venkatesh et al.[9] Topical Diltiazem 2% is found to be equally effective as that GTN ointment with fewer side effects as concluded from study by sajid et al published in 2013.[14] Comparable results were also concluded by Behnam Sanei et al,[12] study published in 2009 as complete remission of anal fissure was occurred in 66.7% patients in diltiazem group. All patients in the

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study were warned that they may experience headache as adverse effect after administration of the ointment. Headache is a major problem for patients treated by GTN ointment. Although 46.6 % of patients treated with GTN experienced headache at some point during treatment Headache was present in 3.3% in group A patients and 46.6% in group B patients which was statistically significant and comparable to the studies conducted by Venkatesh et al 2019,[9] in which 46% patients taking GTN suffered from headache and Ansari et al 2020,[13] showing headache in 16% of patients with GTN. Recurrence of anal fissure was assessed in present study at follow up after therapy in both the groups. In group a recurrence was noted in 6.6% of patients and 10% of group B patients which was statistically insignificant.

CONCLUSIONS

Maximum incidence of anal fissure is found in 3rd, 4th and 5th decade of life, which shows that the anal fissure is predominantly belongs to the middle age group. Male population is affected more then females. Predominant symptom of anal fissure is pain followed by bleeding.The most common location of anal fissure is midline posteriorly, followed by midline anteriorly and least common is lateral position.Diltiazem and Nitroglycerin both are equally efficacious in relieving the symptoms and healing of fissure. Topical 2% Diltiazem appeared to be well tolerated and equally efficacious. Diltiazem is associated with fewer side-effects, probably because of minimal systemic absorption.The study has proved the superiority of Diltiazem over Nitroglycerin as far as side effects are concerned in the short term. Thus Chemical sphincterotomy with topical 2 % Diltiazem gel is an effective first-line treatment for anal fissures, achieving symptom relieving and healing rates comparable to those achieved with 0.2 % Nitroglycerin ointment but with relatively few, generally acceptable side effects as compared to distressing adverse effects of nitroglycerin as headache. However further studies are required to reach the final conclusion.

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