COMPARISON OF HEALING RATE OF ANAL FISSURE WITH 0.2% GLYCERYL TRINITRATE OINTMENT VERSUS 2% NIFEDIPINE OINTMENT

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ABSTRACT

Objective: To compare the efficacy of topical 0.2% glyceryl trinitrate (GTN) ointment with 2% Nifedipine ointment in healing of anal fissure.

Study Design: Quasi experimental study.

Place and Duration of Study: Department of Surgery, Combined Military Hospital (CMH) Dera Nawab Sahib, from Oct 2015 to Oct 2016.

Methodology: A total of 330 patients were divided into two groups (group A and group B) with 165 patients in each group using lottery method. Patients in group A were treated with topical application of 0.2% glyceryl trinitrate ointment for four weeks while group B patients were treated with topical 0.2% nifedipine. Patients were followed up after four weeks of initiation of treatment and healing of fissure was assessed. Frequency of healing of fissure in both groups was calculated and compared.

Results: Healing rate of anal fissure was found significantly higher in group B (79.4%) as compared to group A (63.6%). The *p*-value was found to be 0.002 which was statistically significant. However, gender had no effect on fissure healing (*p*-value 0.413).

Conclusion: Topical 2% nifedipine ointment therapy was superior to 0.2% glyceryl trinitrate ointment in terms of healing of anal fissure.

Keywords: Anal Fissure, Topical 0.2% glyceryl trinitrate ointment, 2% Nifedipine ointment.

INTRODUCTON

Anal fissure is a linear ulcer in the anal canal, distal to the dentate line[1]. It is a frequent and disabling disease, affecting both genders and especially young adults[2]. Anal fissure can be classified into chronic and acute form of fissures. Chronic anal fissure is characterized by the presence of indurated edges, visible fibers of internal anal sphincter at the base of the fissure and sentinel polyp or tag at the distal end of the fissure[3,4]. Increased resting internal sphincter tone is the major factor contributing to non-healing of the fissure. Any treatment which can reduce resting sphincter tone effectively will result in fissure healing. Common modes to reduce internal anal sphincter tone include chemical sphincterotomy and surgical sphincterotomy.

Chemical sphincterotomy can be achieved with use of topical agents including Nitrates (isosorbide dinitrate), calcium channel blockers (diltiazem/nifedipine) or botulinum toxin[5-7]. Chemical sphincterotomy is always added on with change in dietary habits, use of stool softeners and increase in fluid intake to reduce repeated trauma to anal canal by hard fecal matter. In addition to these pharmacological agents, recently; natural agents such as egg yolk are also being used with minimal side effects[8]. Successful chemical sphincterotomy is cost effective, compliant and results in prompt relief of symptoms. However, recurrence rates with use of chemical sphincterotomy is high and surgical sphincterotomy is still accepted as gold standard for treatment of chronic anal fissures when medical management has failed to provide long term relief of symptoms[9].

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Multiple trials have been carried out all around the world to identify most effective agent to reduce internal anal sphincter tone. Local data suggests that diltiazem has better outcome (80.4%) in terms of healing of chronic anal fissure and reductions in symptoms when compared with GTN (62%)[10]. While most studies focus on comparison of diltiazem with other pharmacological agents, we studied to compare nifedipine with GTN to identify the agent most effective in treating anal fissures. Local data of effectiveness of nifedipine is non-existent and our study helped in choosing the more potent agent for effective treatment of anal fissures. Trials carried out for comparison of nifedipine to GTN in Iran revealed nifedipine to be more effective and results were found comparable to our results carried out on local population[9]. The objective of our study was to compare the effectiveness of topical GTN versus nifedipine in terms of fissure healing rate.

METHODOLOGY

This study was carried out at CMH Dera Nawab Sahib (DNS) for 12 months from October 31st, 2015 to October 30th, 2016. Sample size was calculated using WHO Sample size calculator (confidence level 95%, Power = 80%). Sampling technique was non-probability consecutive sampling. A total of 330 patients were included in the study. Approval from institutional ethical committee was obtained and informed written consent was taken from every individual. Every patient reporting to outpatient department (OPD) of Surgery, CMH DNS, planned to be treated conservatively for anal fissure was included. All patients having anal fissure meeting the inclusion criteria that was patients between 20-75 years of age of both genders were randomly distributed in group A and B by lottery method. Patients having anal fistula, metastatic disease, chronic liver disease, chron's disease, diabetes mellitus and patients using steroids were excluded from study. Group A patients were treated with local glyceryl trinitrate ointment for four weeks while group B patients were treated with nifedipine ointment for four weeks. Ointment was applied 12 hourly by all individuals. Patients were followed up after 01 month of initial treatment for pain and bleeding. No oral analgesics were given to patients. Patients with no bleeding and pain were considered to be successfully treated. Presence of either of the residual symptom was considered treatment failure. Observer bias was minimized by observation by same doctor on first day and after one month. Sampling Bias was reduced by randomizing patients to both groups by Lottery method. Data was analyzed using special package for social sciences (SPSS) v 20. Mean and standard deviation was calculated for quantitative variables like age. For categorical variables like gender and efficacy, frequency was calculated. Independent sample t-test was used for comparison of mean age between groups. Chi-square test was applied to compare efficacy of both groups. A *p*-value of ≤0.05 was considered significant.

RESULTS

A total of 330 patients undergoing medical management of anal fissure were recruited and were randomly divided into two equal groups of 165 each. The age distribution ranged from 19-70 years in the study. Minimum age was 19 years and maximum age was 70 years with mean age of 42.11 ± 9.98 years. Mean age in group A was 41.70 ± 10.23 years while mean age in group B was 42.53 ± 9.70 years (*p*-value 0.45). Out of total 330 patients, 192 (58.2%) were males and 138 (41.8%) were females. Among 192 males, 134 individuals

Table-I : Comparison of male versus female in terms of fissure healing (*p*=0.413).

Fissure Healing	Gender		*p*-value
	Male n (%)	Female n (%)	
Yes	134 (69.8)	102 (73.9)	0.413
No	58 (30.2)	36 (26.1)	

Table-II: Comparison of nifedipine versus GTN in terms of frequency of fissure healing (*p*=0.002).

Fissure Healing	Study Group		*p*-value
	Group A (0.2% GTN) n (%)	Group B (0.2% nifedipine) n (%)	
Yes	105 (63.6)	131 (79.4)	0.002
No	60 (36.4)	34 (20.6)	

were successfully treated; while among 138 females, fissure healing occurred in 102 with an insignificant *p*-value of 0.413 (table-I). Group A had 99 (60%) males and 66 (40%) females. Out of 99 males, fissure healing occurred in 59 (59.5%), while out of 66 females, healing occurred in 46 (69.6%) (*p*-value 0.186). Group B had 93 (56.4%) males and 72 (43.6%) females. Out of 93 males, fissure healing occurred in 75 (80.6%), while out of 72 females, healing occurred in 56 (77.8%) (*p*-value 0.655). Fissure healing was checked 30th day of initiation of treatment. Group A revealed 63.6% healing rate as compared to group B which showed healing in 131 (79.39%). The groups had a statistically significant difference in the frequency of fissure healing with a *p*-value of 0.002. Comparison between frequencies is given in table-II.

DISCUSSION

Anal fissure is an ulceration of the anoderm in the anal canal. Its pathogenesis is due to multiple factors: mechanical trauma, sphincter spasm, and ischemia[11,12]. Fissure can cause severe pain and bleeding. Diagnosis is usually made by history and local inspection[13]. Treatment of this condition is aimed at relieving symptoms alongwith eliminating the causative factors. Focus is usually kept on relieving the sphincter spasm which would result in early healing of the fissure by increasing the blood supply of the effected tissue.

Sphincter spasm can be relieved by various methods which include pharmacological and surgical therapies. Use of topical pharmacological agents help reducing internal anal sphincter tone termed as chemical sphincterotomy. Oral use of diltiazem (calcium channel blocker) was suggested in some studies but no trial was found comparing it to its topical use, thus limiting its routine oral use[14]. Most commonly used topical pharmacological agents used to treat anal fissure include GTN, nifedipine/diltiazem and botulinum[15]. Topical GTN ointment is effective in reducing anal sphincter tone and has been used in multiple concentrations including 0.1, 0.2 and 0.4%[16]. Multiple randomized controlled trials have been carried out to compare topical GTN therapy to topical nifedipine therapy with varying results in terms of healing rate, headaches and recurrence rates[17]. Moreover, comparative studies have been carried out to compare efficacy of botulinum to traditional topical agents showing healing rates as high as upto 87%[15].

Surgical management is indicated only once conservative measures and pharmacological agents fail in achieving fissure healing. Commonly performed surgical procedures include lateral internal anal sphincterotomy and mucosal anal advancement flaps. Both open and closed techniques are used for performing surgical sphincterotomy. Among them, closed lateral internal sphincterotomy is the treatment of choice for chronic fissures as it is effective, safe, less expensive, and associated with a lower rate of complications than the open sphincterotomy technique[17]. Lateral sphincterotomy is still the gold standard procedure specially with hypertonic sphincters, however when compared to mucosal advancement flaps; it has higher post operative pain and incontinence rate[18].

Ezri *et al* carried out RCTs in 2003 to compare topical nifedipine and topical GTN ointment application in terms of chronic anal fissure healing rate and found out that healing rate was significantly higher with nifedipine (89%) as compared to GTN (58%)[19]. However, compliance to use of GTN was poor as compared to GTN which caused headache/flushing in 45% of cases as compared to nifedipine group (5%)[19]. Recently trials were carried out in Iran and revealed healing rate of 82.5% with application of 0.2% nifedipine which was significantly higher as compared to GTN (60%)[11]. Our results were comparable to trials carried out in Iran. However, side effects of both treatment modalities including headache and flushing were not recorded in our study.

CONCLUSION

There was a tendency for better healing rate of anal fissure in patients treated with topical

application of 0.2% nifedipine than patients treated with 0.2% GTN ointment. Thus topical use of nifedipine is superior to GTN application in terms of healing rate of anal fissure.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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