ORIGINAL ARTICLE

To compare the frequency of healed wound in patients with hemorrhoids after Milligan-Morgan haemorrhoidectomy given 0.2% topical glyceryl trinitrate (GTN) versus placebo

Zeeshan Hyder, Ghansham, Sagheer H Shah, Syed Osama Zohaib ullah

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Abstract

Objective: To compare the frequency of healed wound in patients with hemorrhoids after Milligan-Morgan haemorrhoidectomy given 0.2% topical glyceryl trinitrate (GTN) versus placebo

Setting and duration: Department of surgery ward 26, Jinnah Postgraduate Medical Centre, Karachi. It was carried out in 6 months from feb 2015 to aug 2015.

Study Design: Randomized Clinical Trial

Methodology: there was total of 124 patients with hemorrhoids were included in this study. Patients were randomly allocated into two groups. Sixty two patients were in group A and treated with 0.2% GTN ointment and 62 were in group B and treated with placebo ointment (petroleum Jelly). A proforma was used to document findings, it included demographic information like patient's age, gender, duration of hemorrhoids hospital registration No, group of patient and wound healing at 2weeks post operatively.

Results: Rate of wound infection was significantly high in group B than group A (67.7% vs. 16.1%; p=0.0005).

Conclusion: GTN ointment enhances the healing of post hemorrhoidectomy wounds without significant side effects.

Key words: Hemorrhoids, Milligan-Morgan haemorrhoidectomy, glyceryl trinitrate, wound infection

Jinnah Postgraduate Medical Centre, Karachi
Z Hyder
Ghansham
SH Shah
SOZ Ullah

Correspondence:
Dr Zeeshan Hyder,
Consultant Surgeon,
Ward 26, JPMC, Karacchi.
Pakistan.
Cell: (0092)0333-2066694
mail: drsham84@hotmail.com

Introduction:

Hemorrhoids are a distension of the normal vascular haemorrhoidal cushions.[1] It is equally common in both sexes.[2] Milligan-Morgan haemorrhoidectomy is the most commonly performed procedure for this condition.[3] It is considered as a relatively safe procedure but complications like post-operative pain and delayed wound healing exist. It is associated with considerable discomfort postoperatively and patients have to wait for long time to resume their work.[4]

The haemorrhoidectomy wound lies in an area where proper surgical dressings cannot be applied. Moreover contamination of the wound site by defecation necessitates the continuous cleansing of the area using warm sitz baths, after each defecation. This leads to a delay in wound healing and pain after defecation, hence increases the time required to resume routine work. Topical application of glyceryl trinitrate (GTN) reduces anal canal pressures, improves anodermal blood flow,[5] and hence increase rate of wound healing. Compared with placebo, perianal application of 0.2 percent GTN ointment significantly decreases postoperative pain after hemorrhoidectomy and reduces analgesic requirements in the immediate post-operative period glyceryl trinitrate ointment also achieves more rapid healing of wounds.[6]

Topical use of glyceryl trinitrate after haemorrhoidectomy may reduce spasm and postoperative pain, while improved anodermal blood flow

may accelerate wound healing.[7] Headaches and a subsequent need for non-narcotic medications may limit benefits of nitroglycerin.[8]

Topical application of glyceryl trinitrate was effective in reducing post-operative pain and healing time, but the substantial incidence of side effects may limit its extensive use.[9] Hwang et al in a randomized controlled trial showed that post-operative GTN use lead to completely epitheliazed wound at 3rd week in 42.5% patients in contrast to 19.04% patients who received placebo.[10] An incomplete or delayed wound healing is associated with perianal irritation and feeling of being unwell for a long period which delays return to normal activity.

Wound healing by GTN after Milligan-Morgan haemorrhoidectomy varies from 42.5% to 77% in different studies,[4,9] so there is still controversy for its usage Therefore the rationale for this study is to provide clarity in data therby clear cut decision could be made for its utilization after haemorrhoidectomy for the improvement in the wound healing, which will potentially reduces patient's morbidity and decreases the social and financial cost for the patient and society.

Objective:

To compare the frequency of healed wound in patients with hemorrhoids after Milligan-Morgan haemorrhoidectomy given 0.2% topical glyceryl trinitrate (GTN) versus placebo

Operational definition:

Wound healing: Wound healing was classified according to the following grades:[5]

- Grade 1: Sloughy
- Grade 2: No Granulation
- Grade 3: Granulating
- Grade 4: Epitheliazing
- Grade 5: Compeletely epitheliazed.

For this study grade 4 and 5 was considered as healed wound at the end of 14th post-operative day.

Grade III hemorrhoids: Peri-anal palpable mass, prolapse upon bearing down and requires manual reduction.

Grade IV hemorrhoids: Peri-anal palpable prolapsed mass and cannot be manually reduced

Material and Methods:

Sample size: The sample size was calculated using website Open EPi, Version 2, open source calculator—SSCohort(http://www.openepi.com/SampleSize/SSCohort.htm). Taking proportions of wound healing as (0.425 and 0.194)[8] in the study group and control group respectively with 95% confidence interval and 80% power of the test the sample size is 124 patients 62 patients in each group.

Study Design: Randomized clinical trial, carried out at ward 26, Jinnah Postgradute Medical Centre. All patients with un complicated grade III and VI hemorrhoids with age limit of 25 to 60 years included in study. Patients were randomly allocated into group A (study group) and group B (control group) by using random allocation software version 1.00. Patients in both groups was underwent elective hemorrhoidectomy using open technique i.e Milligan Morgan technique. Spinal anesthesia was used in all cases. Standard post-operative management was included four hundred milligram of metronidazole thrice daily, 50 milligram of diclo-fenac sodium twice daily for next three days. All patients were advised stool softner (syrup Cremaffin, 2 tsp thrice daily) and sitz bath for 15 minutes twice daily.

In group A, patients were advised to apply 0.2% GTN ointment by his /her finger tip to the anal region thrice daily for 14 days. First dose were applied in the ward on next morning of surgery. In group B, patients were advised to apply placebo ointment (petroleum jelly) accordingly. For assessment, patients were advised to follow after 2 weeks of operation. Their wound was examined and the extent of wound healing determined on the basis of above mentioned criteria. All patients were interviewed to ensure compliance (more than or equal to 80% adherence to the advise was considered as compliance).

A proforma was used to document findings, it was included demographic information like

Table 1: Comparison of final outcome (Wound infection after 2 weeks) between groups

Wound infection	Group A	Group B	P-Value
Yes	10(16.1%)	42(67.7%)	0.0005
No	52(83.9%)	20(32.3%)	

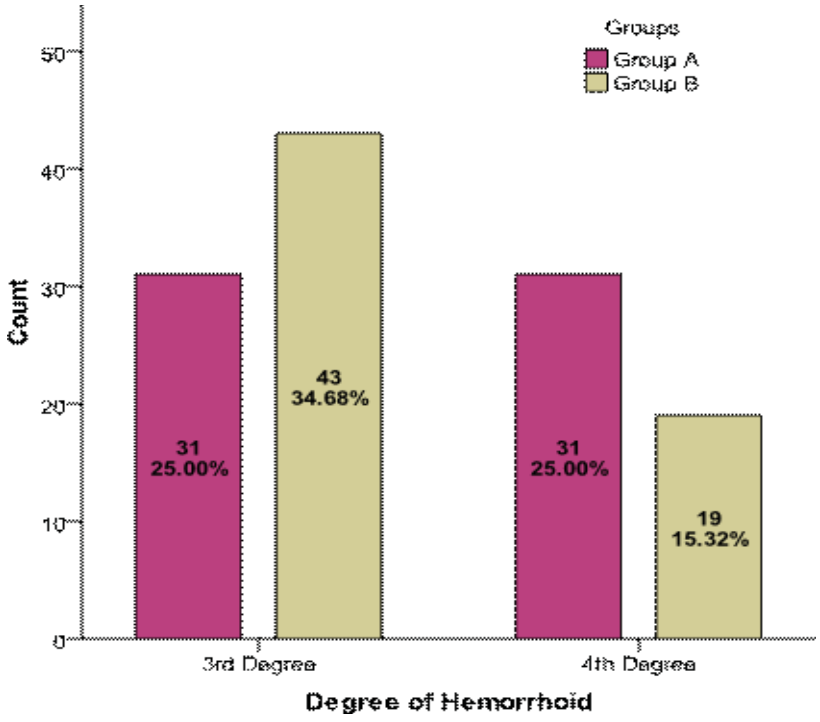
*Chi-square= 33.91; *p≤0.05 significant*

Table 2: Comparison of final outcome (Wound infection after 2 weeks) between groups with respect to grade of Hemorrhoid

Grade of Hemorrhoid	Wound Infection	Group A	Group B	P-Value
3rd Degree	Yes	2(6.5%)	27(62.8%)	
	No	29(93.5%)	16(37.2%)	0.0005
	Total	31	43	
4th Degree	Yes	8(25.8%)	15(78.9%)	
	No	23(74.3%)	4(21.1%)	0.0005
	Total	31	19	

*Chi-Square Test ; *p≤0.05 significant*

Figure 1: Degree of Hemorrhoid with respect to groups (n=124)

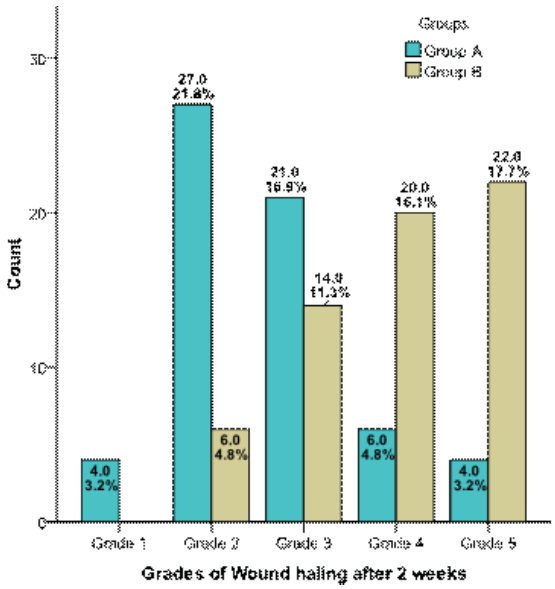


patient's age, gender, duration of hemorrhoids hospital registration No, group of patient and wound healing at 2weeks post operatively.

Data analysis procedure:

Statistical analysis was performed using statistical software SPSS version 16 on computer. Mean ± standard deviation were computed for numerical variables like age.

Figure 2: Grade of wound healing with respect to groups (n=124)



Frequency and percentage were computed for categorical variables like gender, degree of hemorrhoids, wound healing grading and wound healed. Chi-square test was applied to compare the healed wound post Milligan-Morgan haemorroidectomy in two groups (0.2% Glyceryl trinitrate and placebo). The statistical significance was set on P-value ≤ 0.05.stratification was done with regards degree of hemorrhoids to see the effect of these variables on outcome, chi square test was applied.

Results:

A total of 124 patients with hemorrhoids were included in this study. Patients were randomly allocated into two groups. Sixty two patients were in group A and treated with 0.2% GTN ointment and 62 were in group B and treated with placebo ointment (petroleum Jelly).

Out of 124 cases, 76(61.3%) were male and 48(38.7%) female. Regarding degree of hemorrhoid, 74(59.7%) had 3rd degree and 50(40.3%) had 4th degree hemorrhoid (figure 1). Rate of wound infection was significantly high in group B than group A (67.7% vs. 16.1%; p=0.0005) as presented in table 1. significant difference was observed between groups for all age groups (p<0.05) similarly rate of wound infection was significantly high in group B than group A and

for degree of hemorrhoid presented in table 2.

Discussion:

High anal canal pressure is common in patients who have symptomatic hemorrhoids.[11] Galizia et al.[12] recommended a lateral internal sphincterotomy during the hemorrhoidectomy to normalize the anal pressure. However, whether this over activity of the anal sphincter is a cause or an effect of hemorrhoids is not known.[13]

The GTN ointment was introduced as a smooth muscle relaxant and has recently played a role in the management of the anal fissure. Therefore, the concept of a chemical sphincterotomy has taken form as a way to avoid postoperative incontinence.[14,15] The application of GTN leads to nitric oxide–mediated relaxation of the internal anal sphincter[4] and to a decrease in the anal resting pressure of 20 to 40 percent without any symptoms of incontinence.[16] The GTN ointment mainly acts on the upper two-thirds of the anal canal and, to a lesser extent, on the lower one-third of the anal canal and increases the local blood flow for healing.

In this study the average age of the patients was 37.9±7.7 years. Mean age and duration of hemorrhoid were not significant between groups.

Wound healing by GTN after Milligan-Morgan haemorrhoidectomy varies from 42.5% to 77% in different studies,[4,9] so there is still controversy for its usage. In this study rate of wound infection was significantly high in GTN group than placebo group (67.7% vs. 16.1%; p=0.0005). Hwang et al[10] in a randomized controlled trial showed that post-operative GTN use lead to completely epithelized wound at 3rd week in 42.5% patients in contrast to 19.04% patients who received placebo.

Similarly, the study by Tan et al.[17] showed a rate of wound healing consistently faster in patients who received GTN ointment, with completely epithelialized wounds compared to the placebo group. Furthermore, Karalink et al.[18] showed a significant facilitating effect of GTN ointment on post- haemorrhoidectomy wound healing (76.7 % healing at 3 weeks for GTN vs 46.7 % for placebo, p=00.02).

In the meta-analysis of Ratnasingham et al.[19], on three studies, it has been shown that application of 0.2 % GTN ointment is associated with a significantly improved rate of wound healing at 3 weeks compared to matched placebo controls. A theory is that GTN may works in the same manner as in anal fissures, increasing the anodermal blood flow. Good wound healing is essential to prevent perianal irritation, discharge and pain, dehiscence, bacterial infection and reactionary bleeding.[19] Similar findings have been reported in several studies done using metronidazole. It is believed that the analgesic effect of metronidazole is due to improved wound healing. However, there are other studies such that of Balfour et al.[20], which have shown that metronidazole does not reduce post-operative pain.

More recently, some investigators have exposed the concept of chemical sphincterotomy with topical nitrates. Recent evidences suggest that IAS is innervated by neurons that release nitric oxide (NO); stimulation of these nerves results in the release of NO, which then causes relaxation of the IAS by relaxation of smooth muscle. There are several forms of nitrates such as nitroderm bands used after haemorrhoidectomy to reduce the Internal Anal sphincter (IAS) spasm; however, the ointment is the most commonly available and used form. Ratnasingham et al. in their meta-analysis showed that the post-hemorrhoidectomy use of 0.2% GTN ointment was statistically significant in reducing post-operative pain on days 3 and 7, but not statistically significant in reducing pain on post-operative day 1, probably because the major contributor of pain in the early period post-operatively is due to the surgical trauma.[19]

Conclusions:

GTN ointment enhances the healing of post-hemorrhoidectomy wounds without significant side effects. However, as an analgesic, GTN ointment has no merit. GTN ointment utilization after haemorrhoidectomy for the improvement in the wound healing will potentially reduce pa-

tient's morbidity and decreases the social and financial cost for the patient and society.

Conflict of Interest: None

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Role and contribution of authors:

Dr Zeeshan Hyder, Consultant general surgeon, Ward 26, JPMC. Karachi, did collected the data and wrote the initial writeup

Dr Ghansham, Senior registrar, Ward 26, JPMC, Karachi, collected the references and wrote the discusion

Dr Sagheer H Shah, Prof of Surgery, Ward 26, JPMC, Karachi, gives the final touchup to the whole article.

Dr Syed Osama Zohaib ullah, Postgraduate trainee, Ward 26, JPMC Karachi, helped in collecting the data, referrences and helped in discussion and conclusion writing.

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