

To Compare Effect of Topical Calcium Channel Blocker (Diltiazem) Versus Placebo for Pain Control After Hemorrhoidectomy A Prospective Randomise Case Control Study

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Received: 22-02-2024 / Revised: 05-03-2024 / Accepted: 11-03-2024

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Conflict of interest: Nil

Abstract:

Introduction: Surgical haemorrhoidectomy is indicated for the treatment of third and fourth-degree symptomatic haemorrhoids. However, surgery is associated with severe post-operative pain that is a source of such anxiety that some patients decide not to undergo the operation. Post haemorrhoidectomy pain seems to be significantly associated with a spasm of the internal anal sphincter. Calcium channel blockers (CCB), are effective in reducing anal resting pressure. Therefore, it seems likely that an ointment containing Diltiazem (CCB) may be considered as a treatment that affects one of the supposed causes for pain after haemorrhoidectomy.

Aims: To determine, if application of topical calcium channel blocker (Diltiazem) in post haemorrhoidectomy patients would improve pain control as compared to placebo ointment.

Materials and Methods: This was a prospective randomized case control study. 60 patients with Grade-III and Grade-IV haemorrhoids admitted in Government medical college Kota was randomly divided into two groups, consisting of 30 patients in each group. In group A: Calcium channel blocker (Diltiazem) ointment was applied topically and in Group B: Placebo ointment applied topically after haemorrhoidectomy for postoperative pain relief. Patients were followed up to four weeks and postoperative pain score was assessed in term of visual analogue scale after six hours, 24 hours, 48 hours and seven days after haemorrhoidectomy. Any complications after haemorrhoidectomy were checked.

Results: Our study shows that mean pain score in term of visual analogue scale (VAS) were less in Calcium channel blocker (Diltiazem) group as compared to placebo group and it was statically significant (p-value <0.05). The comparison of mean pain score in Calcium channel blocker (Diltiazem) group and in Placebo group was 7.75 and 8.35 at 6 hours, 6.24 and 7.30 at 24 hours, 3.75 and 5.65 in 48 hours, 1.76 and 3.40 at 7 days respectively. So, pain score suggests that there was less pain score in diltiazem group as compared to placebo group. Mean Postoperative hospital stay was also less in diltiazem group (3.03 days) as compared to placebo group (4.06 days). P-value-0.011

Conclusion: We conclude that perianal application of 2% diltiazem ointment along with standard treatment significantly reduces pain after open haemorrhoidectomy. Therefore, this management strategy should be considered as an adjunct in reducing post haemorrhoidectomy pain along with standard treatment.

Keywords: CCB., Diltiazem.

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Introduction

Haemorrhoids are cushions of sub mucosal tissue containing venules, arterioles, and smooth muscle fibres that are located in the anal canal [1,2]. It is the most common issue that general surgeons handle in clinical practice and has been for generations. For the treatment of third and fourth degree symptomatic hemorrhoids, surgical hemorrhoidectomy is recommended. However, some patients choose not to have surgery because of the intense postoperative

pain that is linked to the procedure and causes them great concern.

Painkillers such as opiates and nonsteroidal anti-inflammatory medications (NSAIDs) are frequently used to manage pain, but their use is limited and frequently causes negative effects. [4] Anorectal manometry has shown that anal pressure is greater in patients with haemorrhoids than in the healthy population. [5] Post haemorrhoidectomy pain seems to

be significantly associated with a spasm of the internal anal sphincter.[6]

The calcium channel blockers (CCB) are effective in reducing anal resting pressure.[7,8] Therefore, it seems likely that an ointment containing Diltiazem (CCB) may be considered as a treatment that affects one of the supposed causes for pain after haemorrhoidectomy.

Our study's objective was to ascertain whether CCB's ability to relax smooth muscle would enhance pain management in patients having Milligan–Morgan hemorrhoidectomy.

Method and Material

This randomised prospective case control study was conducted at department of General surgery Government medical college Kota from May 2020 to May 2021.

Patients of both gender who fulfil the inclusion criteria and between 25-65 year of age with third and fourth degree haemorrhoids (according to American society of colon and rectum surgery Classification) were enrolled in this study. Sixty patients with third or fourth degree haemorrhoids who admitted in general surgery department were randomly allocated to treatment by topical 2% Diltiazem (study group) and topical placebo (control group) after Milligan Morgan haemorrhoidectomy.

There were thirty patients in each group. The patients in both groups had previously had elective hemorrhoidectomy assisted by the Milligan Morgan approach. Spinal anaesthesia was used in each case. The anaesthetic drug was administered at the same dosage to every subject.

Both groups of patients received standard postoperative care. Among these were ofloxacin and Ornidazole (twice daily for seven days); analgesia

administered as injections of Diclofenac sodium I/M for one day, followed by three days of taking 50 mg tablets three times a day.

All patients were advised stool softener (syp lactulose, 30ml at bed time) and warm sitz bath for 15 minutes twice daily after immediate postoperative day. In study group, patients were advised to apply 2% Diltiazem ointment by his/her fingertip to the per-rectal region twice daily for 7 days. First dose was applied immediate postoperatively by surgeon himself followed by per-rectal packing. In control group, patients were advised to apply placebo ointment (petroleum jelly) accordingly. All patients were evaluated at 6 hrs, 24 hrs, 48 hrs and 7th day postoperatively for assessment of pain and any complications.

A visual analogue scale was used to quantify postoperative discomfort. The patient was asked to draw a line on the chart representing their estimated level of discomfort. The value in centimetres was then calculated by comparing the drawn line to a standard 10 cm scale. The line's zero end denoted "no pain," while the ten end stood for "severe pain."

Statistical Analysis

Microsoft Excel was utilised for statistical analysis. The distribution of gender and other categorical characteristics were summarised using frequencies and percentages. For numerical data such as the distribution of ages and the mean pain scores, the mean and standard deviation were calculated. The mean pain scores of the study and control groups were compared using the unpaired student t-test. Frequency and categorical variable were compared by use of Chi square test. P value < 0.05 was taken as significant.

Result

Table 1: Age distribution of patients undergoing haemorrhoidectomy

Age group	Diltiazem group(n=30)	Placebo group(n=30)	Total (n=60)
21-30	04 (13.34%)	02 (6.66%)	06 (10.00%)
31-40	09 (30.00%)	08 (26.67%)	17 (28.34%)
41-50	10 (33.32%)	14 (46.66%)	24 (40.00%)
51-60	03 (10.00%)	04 (13.34%)	07 (11.66%)
61-70	04 (13.34%)	02 (6.66%)	06 (10.00%)

In this study the maximum number of patients are from 4th and 5th decade (68.34%) and the mean age of patients in diltiazem group was 43± 10.5 years and in placebo group 44.50±9.06 years.

Table 2: Shows Sex distribution of patients undergoing haemorrhoidectomy

Gender	Diltiazem Group(n=30)	Placebo Group(n=30)
Male	20	22
Female	10	8

P-value=0.57

The total number of males are 42 (70%) and females were 18 (30%).

The CCB (Diltiazem) group having 66.60% males and 33.40 were females and in the Placebo group 73.30% were males and 26.70% were females. The difference was not significant. Overall Male to female ratio was 2.33:1.

Table 3: Post operative pain score in visual analogue scale (mean ± standard deviation.)

VAS	Diltiazem Group MEAN±SD	Placebo Group MEAN±SD	P Value
At 6 Hours	7.75±0.92	8.35±0.69	0.1356
At 24Hours	6.24±0.70	7.30±0.80	<0.001
At ±48Hours	3.75±0.87	5.64±0.76	<0.001
At 7 Days	1.76±0.60	3.40±0.68	<0.001

In our study, We found a statistically significant reduction in post operative pain after hemorrhoidectomy from the first day in the group treated with topical diltiazem 2%, with a mean VAS value of 6.24 +/- 0.70 and a value of 7.30 +/- 0.80 for the Placebo group (p < 0.001, 95% CI) at 24 hrs. We observed that this effect was maintained for the 7

days of the study with mean VAS values on day 2 and day 7 of 3.75 +/- 0.87 and 1.76 +/- 0.60 respectively in the group treated with diltiazem, and of 5.65 +/- 0.76 and 3.40 +/- 0.68 respectively in the placebo group (p < 0.001). Due to persisting effect of spinal anaesthesia there was insignificant difference between VAS score at first 6 hours.

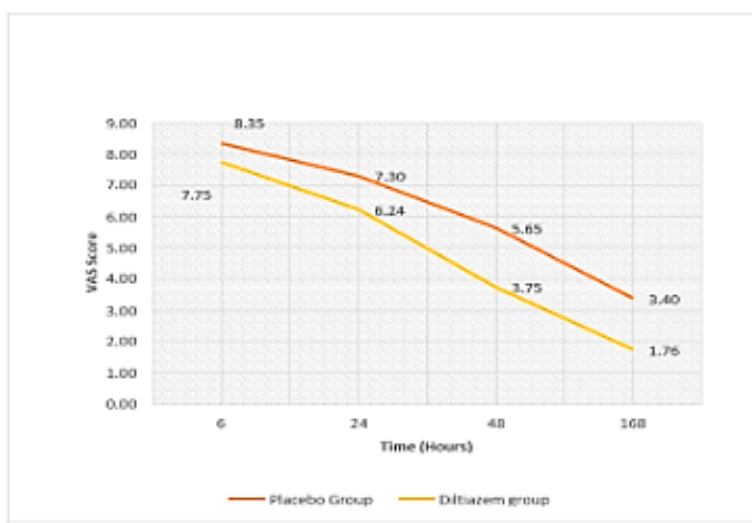


Figure 1: Change in Mean Postoperative Pain Score with Time

Table 4: Comparison of Time to return normal activity

Return tonormal activity	Diltiazem group		Placebo group		Total
	Number	Percentage	Number	Percentage	
0-7 Days	04	(13.33%)	03	(10.00%)	07
8-14 Days	21	(70.00%)	07	(23.34%)	28
>14Days	05	(16.67%)	20	(66.66%)	25

P-Value-0.00031

The normal time to return to normal activity in this study was 10.2± 3.27 days in Diltiazem group and 14.56± 3.10 days in Placebo group. The difference was statistically significant (P value-<0.0001)

Discussion

Haemorrhoids are common disease of population. It commonly affect the people’s of age between 40-60 years. Although haemorrhoids are not life threatening but can cause unhappiness, so it deserve serious examination and treatment.

Haemorrhoidectomy is accepted method of treatment of symptomatic large Piles. It is the best option for grade 3 and grade 4 haemorrhoids, but is associated with significant postoperative pain. Management of

postoperative pain is essential for good postoperative recovery. To relieve this pain NSAIDs and other analgesics like opiates are used but they have their side effect and short time of action. Postoperative pain is associated with spasm of internal anal sphincter. Calcium channel blockers like diltiazem are effective in reducing the anal resting pressure.

In this study maximum number of patients with haemorrhoids were between 41- 50 years of age (40%), the youngest subject being 27 years and oldest 67 years.

Johanson et al.[7] in 1990 in their epidemiological study showed peak prevalence occurred between age 45-65 years and the development of

haemorrhoids before the age of 20 years was unusual. In our study Mean age of patients in diltiazem group was 43 ± 10.5 years and in placebo group 44.50 ± 9.06 years. Silverman et al.[8] (2005) studied pain control after haemorrhoidectomy in patients, in which they divided patients in 2 group. The mean age was 44 ± 16 years in CCB group and placebo mean age was 45 ± 5 years. Rodríguez-Wong et al.[9], Amoli et al.[10] and Yan-Jiun Huang et al.[11] evaluated the role of topical 2% DILTIAZEM application after haemorrhoidectomy and concluded that perianal application of DILTIAZEM ointment after haemorrhoidectomy significantly reduces postoperative pain and is perceived as beneficial with no increase in associated morbidity.

In our study, We found a statistically significant reduction in postoperative pain after hemorrhoidectomy from the first day in the group treated with topical diltiazem at 2%, with a mean VAS value of 6.24 ± 0.70 and a value of 7.30 ± 0.80 for the Placebo group ($p < 0.001$) at 24 hrs. We observed that this effect was maintained for the 7 days of the study with mean VAS values on day 2 and day 7 of 3.75 ± 0.87 and 1.76 ± 0.60 respectively in the group treated with diltiazem, and of 5.65 ± 0.76 and 3.40 ± 0.68 respectively in the placebo group ($p < 0.001$). The statistically insignificant difference between mean VAS score at 6 hours between diltiazem and placebo group can be explained by the persisting effect of spinal anaesthesia in patients postoperatively.

For the purpose of controlling postoperative pain, Chauhan et al.[12] compared topical diltiazem at 2% with internal lateral sphincterotomy in a randomised, prospective research involving postoperative hemorrhoidectomy patients. Although the authors concluded that lateral sphincterotomy reduced postoperative pain more than diltiazem, a higher rate of complications may restrict the applicability of sphincterotomy as a pain management strategy after hemorrhoidectomy.

Our study shows that the Diltiazem group patients returned to their normal activity significantly early with mean of $10.2 (\pm 3.27)$ days as compared to the Placebo group with mean of $14.56 (\pm 3.10)$ days. Time to return to normal activity was significantly earlier in Diltiazem group with P-value < 0.001 . About 13.33% returned to normal activity within 7 days in Diltiazem group as compared the Placebo group in which 10% patients who returned to their normal activity within 7 days.

Conclusion

Post haemorrhoidectomy pain remains a common problem in surgery for which NSAIDs and narcotic analgesics are generally required. In our study, we compare the effect of topical Diltiazem for pain control after haemorrhoidectomy, and we found that

pain score in VAS is significantly low as compared to placebo ointment. So application of topical 2% diltiazem reduced postoperative pain in the patients undergoing haemorrhoidectomy, compared to placebo group, with no increase in associated morbidity. The results were clinically and statistically significant.

Based on our finding we find that perianal application of 2% diltiazem ointment along with standard treatment are better option for pain control pain after open haemorrhoidectomy. Therefore, this management strategy should be considered as an adjunct in reducing post haemorrhoidectomy pain along with standard treatment.

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