

A comparative study of diclofenac suppository versus topical 2% diltiazem gel in post-operative pain relief after open hemorrhoidectomy

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Abstract

Hemorrhoids are one of the most common anorectal diseases. Hemorrhoidectomy still stands as the most effective treatment for high grade hemorrhoids and postoperative acute pain as an expected result of hemorrhoidectomy has been experienced by thousands of patients all over the world and hence its only obstacle. Pain control using various invasive and noninvasive methods after hemorrhoidectomy has been constantly under debate and investigation. During the study period, 100 consecutive patients undergoing open hemorrhoidectomy under spinal anesthesia are allotted alternatively to each group. So 50 patients in each group of topical 2% diltiazem and diclofenac suppository. The diltiazem group yielded the lowest visual analog scale (VAS) score on post-operative day zero after surgery ($p < 0.05$). The diclofenac group reported the lowest VAS score on following post-operative day one, two after surgery ($p < 0.05$). There were no complications after treatment with either of these drugs. Topical use of diltiazem gel is appropriate for short-term pain control following hemorrhoidectomy, while diclofenac yields a more sustainable pain control.

Keywords: Open hemorrhoidectomy, diltiazem, diclofenac, visual analog scale, post-operative pain

Introduction

The word 'Hemorrhoid' is derived from Greek, meaning flowing of blood (haem=blood, rhoos=flowing). The word 'piles' comes from Latin word pila meaning a pill or ball. To be accurate, we should call the disease as piles when the patient complains of a swelling and 'hemorrhoids' when he or she complains of bleeding ^[1].

Hemorrhoidectomy still stands as the most effective treatment for high grade hemorrhoids and postoperative acute pain as an expected result of hemorrhoidectomy has been its only major problem. The reason for delayed patient discharge after hemorrhoidectomy is commonly due to post-operative pain. Moreover, this matter is important because it involves both cost and social issues in terms of bed occupancy and delayed return to work ^[2]

The cause of post-hemorrhoidectomy pain is multifactorial, including spasm of anal sphincter and puborectalis muscles, type of anesthesia, poor and delayed wound healing, surgical technique, type of post-operative analgesia, use of stools softeners and subjective pain threshold have been implicated as potential mechanisms. Pain control after hemorrhoidectomy has been constantly under debate and investigation. Pain after hemorrhoidectomy is great suffering for patients and challenging for surgeons ^[2].

Various invasive and noninvasive methods, including sphincterotomy, anal dilation,

application of topical preparations, flavonoids and oral or parenteral analgesics have been suggested to relieve internal sphincter spasm to resolve post hemorrhoidectomy pain. Topical preparations are preferred because of better bioavailability and fewer incidence of adverse events compared with other dosage forms^[3,4].

In this study, management of post hemorrhoidectomy pain relief by diclofenac suppository and topical diltiazem gel in patients has been evaluated and compared.

Methodology

A written informed consent will be taken from all patients included in the study. Patients who are chosen will be explained of the various options available for the treatment of hemorrhoids along with their advantages and disadvantages and they are allowed to choose the line of treatment they preferred. Detailed history taking, thorough clinical examination and investigations will be done for these patients.

Inclusion criteria

- All consenting patients aged between 20 years to 60 years.
- Patients who are diagnosed with grade three and four internal hemorrhoids and hemorrhoids that have not been cured by non-operative treatments.
- **Intervention:** Open hemorrhoidectomy under spinal anesthesia.
- Available for follow-up.

Exclusion criteria

- Secondary internal hemorrhoids and co-morbid conditions like ascites, portal hypertension, uterine pathology, anorectal carcinoma, neurological like paraplegia etc.
- Patients with coagulation disorders, renal disease, peptic ulcer disease, asthma or known allergies to non-steroidal anti-inflammatory drugs (NSAIDs).
- Current calcium channel blocker uses or known side-effects from previous calcium channel blocker use; severe hypertension, orthostatic hypotension; History of ischemic heart disease.
- Pregnancy.

Method of application of diltiazem 2% Gel

After hemorrhoidectomy patients were instructed to squeeze 1 cm of the gel (*0.5 g) from the dispenser onto a finger and apply this three times a day to their perianal region and at least 1.5 cm into anus for 14 days. The first dose was applied by the surgeon at the completion of the hemorrhoidectomy. Perioperative management was standardized. Water intake and diet were resumed on the day of the operation.

Method of insertion of diclofenac 100 mg suppository

After hemorrhoidectomy patients were instructed to insert diclofenac 100 mg suppository two times a day, at least 1.5 cm into anus for 14 days. The first dose was applied by the surgeon at the completion of the hemorrhoidectomy. Perioperative management was standardized. Water intake and diet were resumed on the day of the operation.

The data collected will be entered into a specially designed case record form to record their data, including their age, gender, duration of surgery, intensity of pain at different times after surgery, the interval to the first administration of opioids and the overall amount of opioid used.

The pain intensity was measured using a visual analog scale (VAS), in which a ruler graded from one to ten was shown to the patients so that they could indicate the amount of pain they felt (zero being pain free and ten being the greatest pain they have ever felt). Pain measurements were performed upon the patient's transfer to the recovery ward, on the day-0, 1, 2 and 3, respectively. Any measurement of pain above three in the VAS method was considered to be the occurrence of pain.

Results

There were no significant differences between the two groups with regard to hemorrhoid grades and quadrants excised.

Table 1: Comparison between Group and Hemorrhoids Grade

| | Grade 3 | Grade 4 |
|-------------------------------|---------|---------|
| Diclofenac 100 Mg Suppository | 26 | 24 |
| Diltiazem 2% Gel | 28 | 22 |

The postoperative pain scores, measured by VAS, tended to be lower in the diltiazem group compared to diclofenac group (p-value < 0.05, Kruskal-Wallis rank sum test).

Table 2: Comparison between Group and VAS POD 0

| | Average | Standard Deviation | P. value |
|-------------------------------|---------|--------------------|----------|
| Diclofenac 100 Mg Suppository | 4.64 | 0.92 | < 0.05 |
| Diltiazem 2% Gel | 3.62 | 0.97 | |

The postoperative pain scores, measured by VAS, tended to be lower in the diclofenac group compared to diltiazem group (p-value: 0.003736, Kruskal-Wallis rank sum test) which is significant.

Table 3: Comparison between Group and VAS POD 1

| | Average | Standard Deviation | P. value |
|-------------------------------|---------|--------------------|----------|
| Diclofenac 100 Mg Suppository | 3 | 0.9 | 0.003736 |
| Diltiazem 2% Gel | 3.46 | 0.68 | |

The postoperative pain scores, measured by VAS, tended to be lower in the diclofenac group compared to diltiazem group (p-value < 0.05, Kruskal-Wallis rank sum test) which is significant.

Table 4: Comparison between Group and VAS POD 2

| | Average | Standard Deviation | P. value |
|-------------------------------|---------|--------------------|----------|
| Diclofenac 100 Mg Suppository | 2.52 | 0.74 | 0.05 |
| Diltiazem 2% Gel | 3.2 | 0.64 | |

The postoperative pain scores, measured by VAS, tended to be almost similar both groups (p-value = 0, Kruskal-Wallis rank sum test).

Table 5: Comparison between Group and VAS POD 3

| | Average | Standard Deviation | P. value |
|-------------------------------|---------|--------------------|----------|
| Diclofenac 100 Mg Suppository | 2.2 | 0.61 | 0 |
| Diltiazem 2% Gel | 2.88 | 0.59 | |

Complications

Diclofenac Suppository Group

- No complications were reported after follow up of patients for 1 month.

Diltiazem Gel Group

- No complications were reported after 1 month.

Overall both groups didn't present drug related complications which compelled to discontinue the drug or didn't require any additional management.

Discussion

There is no similar study has been conducted to compare the pain-reducing effects of a diclofenac suppository versus diltiazem gel after hemorrhoidectomy. But previous studies indicated that NSAID use reduced the need for opioids after surgery, helping patients to avoid the adverse effects of opioids.

In a study by Lyons *et al.* [5] on the effect of a diclofenac suppository on pain after venous varicosis surgery, it was noted that the prostaglandin release peaked at about 3-4 h after surgical trauma and the NSAIDs could inhibit the pain stimulus caused by this prostaglandin release. Similarly, our study indicated the diclofenac suppository to have less analgesic effect compared to diltiazem gel at the time of transfer to recovery and post-op day zero after surgery, which was in agreement with the above study.

The spasm-relieving effect of diclofenac may account for its more sustainable pain reduction, as it has been assumed that the main underlying reason for post-hemorrhoidectomy pain is spasm of the internal anal sphincter. Mojgan Rahimi *et al.* [6] evaluated 90 patients were recruited for this randomized clinical trial and were randomly categorized into three groups (30 patients in each group). After surgery, the patients in the first group received one 100 mg diclofenac suppository, those in the second group received 5g of EMLA and those in the third group received 5g of petrolatum ointment (control group). The pain intensity was measured using a visual analog scale (VAS). They concluded that topical use of an EMLA cream is appropriate for short-term pain control following hemorrhoidectomy, while diclofenac yields a more sustainable pain control. This study only examined the period of 24 h after surgery, which may not be an adequate length of time studied to claim that diclofenac resulted in "long-term" pain control [7].

Huang Y-J *et al.* [2]. Did meta-analysis of patients who underwent hemorrhoidectomy using topical diltiazem ointment versus placebo (Vaseline) for pain control. Patients with third or fourth degree hemorrhoids undergoing traditional hemorrhoidectomy were included. Procedures took place in the colorectal division of a hospital in 5 countries. Five randomized control trials (RCTs) published between 2005 and 2016 including 227 patients were included our meta-analysis (Diltiazem (calcium channel block) group Z 137; Placebo (Vaseline) group Z 90). Pain assessment was performed using a standardized Visual Analogue Scale. The results revealed that Diltiazem ointment was statistically significant in reducing pain within 48 h, at 72 h, and more than 96 h after operation compared to the placebo group. Regarding overall complications (including headache), there was no statistical significance between diltiazem and placebo group [2].

The duration of action of topical diltiazem is also likely to be important issue. Carapeti *et al.* [8] study on topical diltiazem ointment shows that lower anal pressures can be maintained significantly for up to 5 h in healthy volunteers. By causing a more sustained reduction in anal pressure after hemorrhoidectomy, the application of diltiazem ointment may reduce anal pressure for longer than Glyceryl trinitrate (GTN) but short duration than diclofenac.

The diltiazem group felt more convenient about usage compared to diclofenac group. It was

known from the studies that the topical applications more convenient than suppository. The administration of tramadol could be a confounding factor in measuring the VAS score in our study, which could not be avoided for ethical reasons. Although the lower pain scores in the diltiazem group upon transfer to recovery on post-op day zero after surgery were statistically significant, the early pain scores could be the result of spinal anesthesia. Therefore, further clinical trials with a larger sample size and distinct groups using different anesthetic techniques will be needed to draw more definitive conclusions.

In our study there were no control groups which managed without use of any of two study drugs. This deficiency puts hindrance to draw definitive conclusions like incidence of breakthrough post-op pain among patients and incidence of complications, patient conveniences and longer follow up about wound healing.

Conclusion

The conclusion of this study is topical use of diltiazem gel is appropriate for short-term pain control following hemorrhoidectomy due to its direct action on internal sphincter tone, while diclofenac yields a more sustainable pain control because of its action on controlling inflammation and also in turn relaxes the sphincter.

Complications in each group are minimal and not significant enough to stop treatment. But patients appear to be more comfortable in using topical gel than the rectal suppository.

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