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Original Article

Randomised clinical trial of effect of oral nifedipine on pain and healing after hemorrhoidectomy

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Abstract. Hemorrhoidectomy has the best long-term results and is the only effective treatment for symptomatic third and fourth degree hemorrhoids. Patients and doctors consider it a painful operation. Nifedipine reduces the activity of the internal anal sphincter and relieves symptoms in patients with haemorrhoids or anal fissure. The aim of this study was to evaluate the effect of oral nifedipine after haemorrhoidectomy.We randomly assigned 40 consecutive patients admitted for hemorrhoidectomy by Milligan Morgan technique. Group 1 (n=20) is the control group, group 2 (n=20) is the study group. All received habitual treatment; lactulose as stool softener, metronidazole 500 mg three times daily for seven postoperative days, and ketorolac tromethamine as analgesic. Group 2 additionally received oral nifedipine 20 mg twice daily from 2 days before surgery until wound healing. Linear analog scales were used to assess pain. Time to first bowel movement, return to normal activity, complications, and use of additional analgesics were recorded. Patients were reviewed and assessed postoperatively every week for measurement of blood pressure, pulse rate, wound healing and adverse effects until return to work. Patients in the oral nifedipine group had significantly less pain, less analgesics consumption [median 18 (12 - 38) *vs* 33 (25 - 48)] (*P*=0,021). Median time to healing the wounds was 28 days (range 14 - 40) in the oral nifedipine group and 40 days (21 - 60) in the control group (*P*=0,023). Median time to return to work or normal activity was 37.5 days (range 20 - 80) in the oral nifedipine group and 47.5 days (20 - 115) in the control group (*P*=0,445). There was no significant change in baseline pulse rate or systolic and diastolic blood pressure. Headache occurred in 4 patients who responded to paracetamol. The use of oral nifedipine reduced postoperative pain, analgesic consumption, and promoted earlier wounds healing and return to work. And we suggest its inclusion in routine posthemorrhoidectomy treatment.

Key words: Nifedipine, hemorrhoids, hemorrhoidectomy, postoperative pain, wound healing

1. Introduction

Hemorrhoidectomy is the most effective treatment for third and fourth degree haemorrhoids (1). Hemorrhoidectomy involves excision of the prolapsed haemorrhoids and is usually associated with severe pain. The control of post-hemorrhoidectomy pain has always been the main concern for the surgeon, and tremendous efforts have been made to reduce the pain in order to render hemorrhoidectomy possible as an ambulatory procedure. There have been attempts to modify the surgical technique, such as using diathermy (2), a harmonic scalpel (3) or Ligasure (4) for the excision of haemorrhoids. With stapled haemorrhoidectomy (5) significant reduction of postoperative pain is achieved. However, long term follow-up shows that results are not durable and fourth degree patients were unsatisfied (6).

Surgical or medical means to reduce sphincter muscle spasm have also been tried to reduce postoperative pain (7-9). Different forms of analgesia and anaesthesia have also been used (10,11). Furthermore, postoperative antibiotics to reduce infection are effective in reducing postoperative pain (12).

Nifedipine has been shown to reduce the activity of the internal anal sphincter and relieve symptoms in patients with haemorrhoids or anal

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Table 1. Characteristics of patients

Groups	No of patients	Hemorrhoid degree 3/4	Mean age (range) (year)	Sex (M/F)	Median anxiety score (range)	Median depression score (range)
Group 1 Habitual treatment only	20	10/10	46.4 (23-71)	12/8	6.5 (0 –34)	5 (0 – 23)
Group 2 Habitual treatment plus oral nifedipine	20	8/12	47.9 (25-65)	11/9	5.5 (0 –32)	4.5 (0 – 25)

Anxiety p = 0,350 - Depression p = 0,386

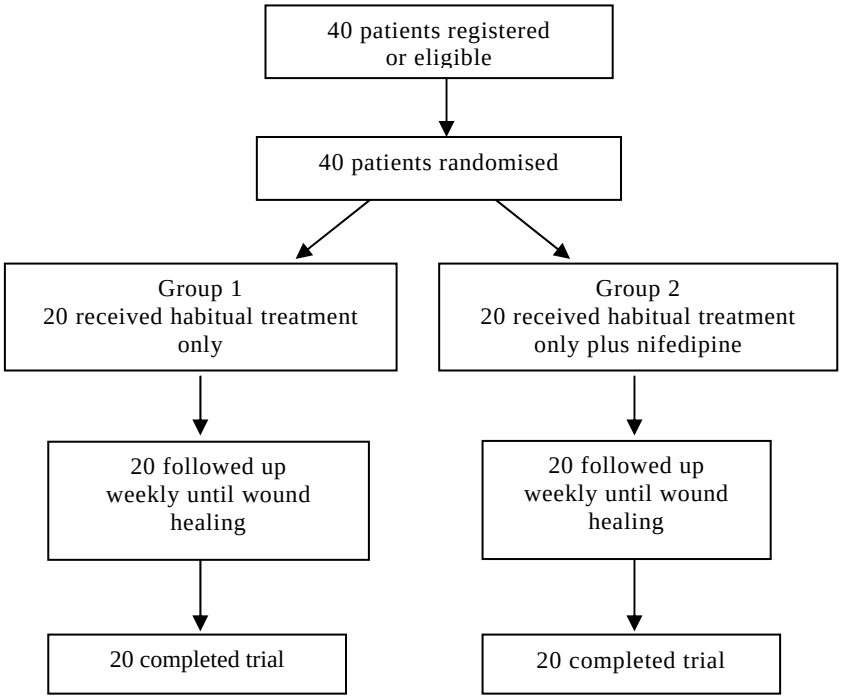

Fig. 1. Trial profile

fissure (13,14). The aim of this study was to evaluate the effect of oral nifedipine after haemorrhoidectomy.

2. Materials and methods

Forty patients with symptomatic third and fourth degree hemorrhoids were recruited from surgical outpatient clinics; individuals with cardiovascular disease, hypertension and those who were pregnant or breast feeding were excluded. For the trial, informed consent was obtained from all patients. They were undergoing haemorrhoidectomy by Milligan Morgan technique. Group 1 (n=20) is the control group, group 2 (n=20) is the study group. All received the habitual treatment; lactulose as stool softener, metronidazole 500 mg three times daily for seven postoperative days, and ketorolac tromethamine

as analgesic, 10 mg up to four times a day as needed. Twenty randomly selected patients (group 2) additionally received oral nifedipine 20 mg twice daily from 2 days before surgery until wound healing (Figure 1).

We supplemented the preoperative consultation with a comprehensive information booklet about hemorrhoidectomy by Milligan Morgan technique. Preoperative assessment included documentation of symptoms, proctoscopy to exclude other pathology in the anus and rectum. All patients received a phosphate enema on the morning of the day of surgery. All operations were performed by the author, using spinal anaesthesia. All patients were discharged home next day. An outpatient clinic appointment was made for one week after surgery and patients were given a telephone number to call for any queries or in case of emergency. They were also asked to keep a diary of additional analgesics used, day of the first postoperative bowel motion and any adverse effects. In addition, patients were asked about the first day of return to work or to full normal activity. The patients were reviewed and assessed at the first visit and every week for measurement of blood pressure, pulse rate, wound healing and adverse effects until return to work.

Patients assessed postoperative pain every day using a 10 cm-linear analogue scale; on which they recorded the pain experienced. To assess whether psychological factors played a role in pain response, patients were asked to complete the Hamilton anxiety and depression questionnaire before surgery.

We used the Mann Whitney *U* test to compare the pain scores between groups. We compared the use of additional analgesics using x^2. We took a value of $p<0.05$ to be significant. We calculated by *t* - test that a sample size of 17 would allow us to show a mean (1SD) difference at 5% significance level and with 80% power. Because we expected to analyse the data by non-parametric tests, we increased the sample size by 10% to 20 patients per group.

Data were collected by nurses.

3. Results

Forty patients underwent hemorrhoidectomy by Milligan Morgan technique during the trial period. Characteristics of patients and preoperative psychological profiles were similar for the two groups (Table 1). The extent of surgery was similar in the two groups, all patients had all three major piles excised. All patients were discharged within 24 h of surgery.

Table 2. Oral nifedipine (group 2)

Treatmat period	Pulse rate (Pulse/min)	Diastolic pressure (mmHg)	Systolic pressure (mmHg)
Pretreatment	75.3 ± 5.29	78.75 ± 8.75	135.25 ± 8.81
Week 1	72.4 ± 4.52	76.15 ± 5.22	132.75 ± 8.50
Week 2	71.2 ± 3.96	75.20 ± 4.86	131.50 ± 8.59
Week 3	70.7 ± 2.27	74.65 ± 5.14	130.35 ± 8.79
Week 4	70.0 ± 1.94	74.70 ± 4.61	129.50 ± 8.41
Week 5	70.0 ±2.05	74.35 ± 4.34	128.25 ± 7.99
Week 6	70.6 ± 2.16	73.45 ± 4.16	127.75 ± 7.69
p> 0.05 compared to pretreatment values			

Pulse rate (pulse / min), diastolic pressure and systolic pressure (mmHg; mean ± SD) values before treatment and at each visit during follow-up in oral nifedipine group until return to full activity

We observed earlier bowel motion in the oral nifedipine group with 16 (80%) patients opening their bowels within 24 h *vs* 7 (35%) patients in control group (p=0,004). The median pain score was highest on days 2 and 3 after surgery (Figure 2). Patients in the oral nifedipine group reported significantly less pain than those in control group (*p*=0.003). Similarly, analysis of the summary scores (for each patient) showed that the oral nifedipine group were free of pain as from dayeight. On average, oral nifedipine group patients consumed less Ketorolac tromethamine tablets than control group, [Median 18 (12–38) *vs* 33.5 (25–48)] (p=0,021), two patients in control group received oral pethidine from their family physician. Four patients in the nifedipine group developed flatus incontinence, which stopped when the oral nifedipine was discontinued. In control group, three patients did not tolerate lactulose and were treated for constipation; two reacting to fibre supplements and senna, while

the third was readmitted to hospital on day 10 with faecal impaction and pain, treated with enemas, and was discharged 24 h later. No one experienced complications. There was no significant change in the pulse rate or systolic and diastolic blood pressure from the baseline readings and throughout the treatment period (Table 2). No patient developed postura l hypotension. Headache occurred in four patients

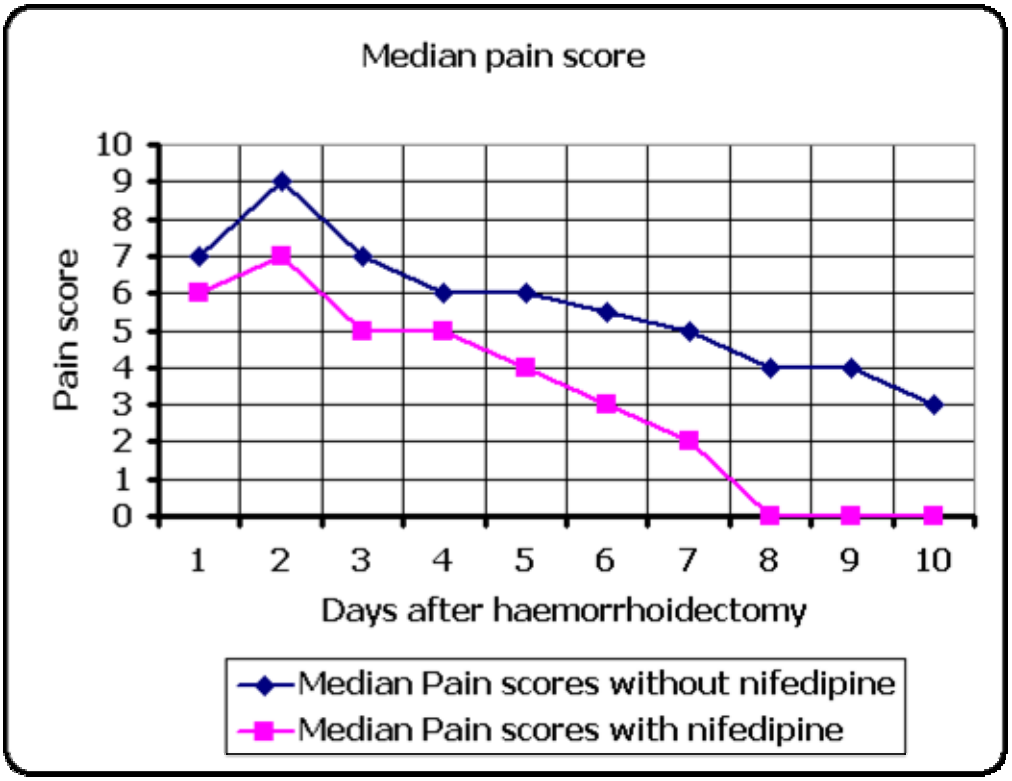

Fig. 2. Median pain score

Table 3. Wound healing time

Procedures	2weeks	3 weeks	4 weeks	>4weeks	
Without oral nifedipine (Group 1)	0	1	4	15	p=0,023
With oral nifedipine (Group 2)	2	3	7	8	

who responded to paracetamol. At the review after four weeks, seven patients from nifedipine group were healed *vs* four patients in control group (Table 3). Median time to healing the wounds was 28 days (range 14-40) in the oral nifedipine group and 40 days (21-60) in the control group (p=0,023). The time to return to work or full normal activity was significantly earlier for patients in the oral nifedipine group [median 37 days (range 20–80)] than for those in control group [47 days (20–115)] (p=0,445). No patients dropped out of the study or were lost to follow-up.

4. Discussion

Various outpatient procedures have been described to treat symptomatic hemorrhoids, which has led to the suggestion that, because of severe postoperative pain, surgery should be reserved for only complicated external hemorrhoids (15-17). Evidence shows that these outpatient procedures have a high initial failure rate, a high rate of recurrence long term (18,19)

and a possible association with occasional adverse and sometimes life-threatening complications (20-22). Hemorrhoidectomy has the best long-term results and is the only effective treatment for third and fourth degree hemorrhoids (1). When performed carefully, recurrent symptoms and complications are rare, but it is usually associated with severe pain. We postulated that the postoperative pain might be due to the sphincter muscle spasm and the wound are the primary causes of pain. It has been demonstrated that tone and spontaneous activity of the internal anal sphincter are dependent upon extracellular calcium and flux across the cell membrane through L-type calcium channels (23-24). Reduction in resting anal pressure was reported using nifedipine (14,25-26). In the present study the calcium channel antagonist nifedipine was used in an attempt to modulate resting anal pressure. We found that nifedipine was associated with a significant reduction in pain score and less analgesic consumption. There were also earlier bowel motions. The healing time and return to work or full normal activity was significantly earlier for patients in the oral nifedipine group than in the control group. Although, we have observed, that the patients in both groups, take a long time to return to paid employment, this may be attributed to Health Service funding.

During treatment period, four patients reported transient headache which was relieved with paracetamol. There was no significant change in the pulse rate or systolic and diastolic blood pressure from the baseline readings and throughout the treatment period. No patient developed postural hypotension and there were four patients who developed flatus incontinence, which stopped when the oral nifedipine was discontinued.

We have conducted a search in pubmed regarding the use of nifedipine in hemorrhoidectomy. Only two works have been published previously. The first one is: Postdefaecation pain syndrome after circular stapled anopexy is abolished by oral nifedipine. In this work, oral nifedipine was added to only three of 77 patients that had residual pain after circular stapled anopexy and rapidly abolished symptoms (27). In the second work topical anorectal nifedipine and lidocaine (lignocaine) ointment was used during postoperative dressing after haemorrhoidectomy without local or systemic adverse events (28).

This trial was not blinded by giving placebo treatment to avoid bias caused by placebo effect. So, the patient knew that he was enrolled in the "experimental" group, to avoid legal conflicts. Is a pioneering study, to avoid that the results of data collected after hemorroidectomy, are biased by the personal opinion of the author. Could be developed by increasing the sample size and with more authors.

However, we can conclude that the use of oral nifedipine reduced postoperative pain, analgesic consumption, and promoted earlier wounds healing and return to work. And we suggest its inclusion in routine posthemorrhoidectomy treatment.

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