How we can improve patients’ comfort after Milligan-Morgan open haemorrhoidectomy

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Received: September 14, 2010 Revised: December 9, 2010 Accepted: December 16, 2010 Published online: March 21, 2011

Abstract

AIM: To demonstrate the value of Diosmin (flavonidic fraction) in the management of post-haemorrhoidectomic symptoms.

METHODS: Eighty-six consecutive patients with grades III and IV acute mixed hemorrhoids admitted to the Anorectal Surgical Department of First Affiliated Hospital, Xinjiang Medical University from April 2009 to April 2010, were enrolled in this study. An observer-blinded, randomized trial was conducted to compare post-haemorrhoidectomic symptoms with use of Diosmin flavonidic fraction vs placebo. Eighty-six patients were randomly allocated to receive Diosmin flavonidic fraction 500 mg for 1 wk (n = 43) or placebo (n = 43). The Milligan-Morgan open haemorrhoidectomy was performed by a standardized diathermy excision method. Pain, bleeding, heaviness, pruritus, wound edema and mucosal discharge were observed after surgery. The postoperative symptoms and hospitalization time were recorded.

RESULTS: The mean age of the Diosmin group and controls was 53.2 and 51.3 years, respectively. In Diosmin group, haemorrhoid piles were of the third degree in 33 patients and the fourth degree in 10; and in the control group, 29 were of the third degree and 14 were of the fourth degree. There was no statistically significance in age, gender distribution, degree and number of excised haemorrhoid piles, and the mean duration of haemorrhoidal disease between the two groups. There was a statistically significant improvement in pain, heaviness, bleeding, pruritus from baseline to the 8th week after operation (P < 0.05). Patients taking Diosmin had a shorter hospitalization stay after surgery (P < 0.05). There was also a significant improvement on the proctoscopic appearance (P < 0.001). However, there was no statistical difference between the two groups in terms of wound mucosal discharge. Two patients experienced minor bleeding at the 8th week in Diosmin group, and underwent surgery.

CONCLUSION: Diosmin is effective in alleviating post-operational symptoms of haemorrhoids. Therefore, it should be considered for the initial treatment after haemorrhoid surgery. However, further prospective randomized trials are needed to confirm the findings of this study.
INTRODUCTION

Hemorrhoid is one of the most common anorectal disorders. Although haemorrhoidectomy is considered as a minor inpatient procedure, it is usually associated with significant postoperative complications, including pain, bleeding, heaviness, pruritus, mucosal discharge and anal stenosis, resulting in a protracted period of recovery. The Milligan-Morgan open haemorrhoidectomy is the most widely practiced surgical approach for the management of hemorrhoids and is considered the “gold standard”. Hemorrhoids are divided into 4 stages depending on symptoms and degree of prolapse. The 3rd and 4th stages are indicated for Milligan-Morgan open haemorrhoidectomy. Hemorrhoidectomy is usually associated with considerable pain, bleeding, and mucosal discharge after operation[1], which seem to be multifactorial, such as individual tolerance, mode of anesthesia, postoperative analgesics, and surgical technique[2].

Pain is a major postoperative complication after haemorrhoidectomy. Although Longo’s procedure (the procedure for prolapse and hemorrhoids, PPH) has been widely used in recent years, it can also be confronted with the postoperative management dilemma after the procedure. A Meta-analysis comparing the PPH procedures and open haemorrhoidectomy did not show any significant differences in terms of post-operative pain. Although the postoperative bleeding and blood loss were significantly lower in the PPH group, there was no statistical difference in the aspect of other complications such as pain, pruritus, and mucosal discharge. In identifying approaches to reduce the symptoms after haemorrhoidectomy, published studies have mainly focused on the choice of surgical technique or the prevention of secondary infection in the wound[3-8]. The superiority of stapled haemorrhoidectomy in terms of less post-operative pain and quicker recovery was confirmed by a more recent systematic review of 25 randomized trials that compared stapled haemorrhoidectomy and conventional haemorrhoidectomy[9]. However, the control of hemorrhoid symptoms is not striking. Both open and closed haemorrhoidectomy have been evaluated in terms of postoperative pain. Two predominant factors responsible for post-operative pain include discomfort from the surgical wound in the sensitive anoderm as well as perianal skin and edema from tissue inflammation around the wound[10]. Alleviation of pain from the surgical incision should be achieved by minimizing tissue dissection and using different electrosurgical devices, such as diathermy, Harmonic scalpel®, and ligature™, which diminishes thermal injury to the subjacent tissues[11]. For reduction of pain from the open wound of haemorrhoidectomy, various kinds of medication, including metronidazole, glyceryl trinitrate (0.2%), steroids, local anesthetics (bupivacaine), anti-inflammatory drugs, hemorrhoid creams, are being used with variable outcome[11-13]. These studies indicated some limitations with these medications such as short duration of action and occurrence of serious side effects.

Postoperative bleeding is another important complication in haemorrhoids due to its frequency, which varies between 0.6% and 10%[14,15]. Post-haemorrhoidectomy bleeding is commonly associated with the passage of a hard stool. Sometimes bleeding may be alarming, because it may cause anemia very rapidly in patients. The causes of post-operative bleeding are not easily explained: in some cases it should be attributed to falling off of a scar due to electrocoagulation, whereas in other cases it is due to the lack of a thrombus, its expulsion or its dissolution, concomitant with the falling or reabsorption of the transfixated stitch.

Diosmin, flavonidic fraction, which is derived from some plants or the flavonoid Hesperidin, is promoted as a high-quality active ingredient in vein improvement supplements. Diosmin reduces inflammation and increases vein tonicity, two important factors that contribute to hemorrhoids. Researches indicate that Diosmin also appears to significantly shorten the duration of haemorrhoid bleeding as well as reduce the postoperative pain[14]. A 2000 Italian study of 66 haemorrhoid patients reported that Diosmin decreased pain by 79% and bleeding by 67% during the first week of treatment, followed by an astonishing 98% and 86% reduction in these symptoms by the second week[17]. After haemorrhoid surgery, flavonoids were found to relieve pain, bleeding and other symptoms more rapidly than standard antibiotic/anti-inflammatory treatment alone, with especially significant symptom relief during the first 3 d after surgery[18].

This study was designed to evaluate the influence of Diosmin on reducing postoperative pain, bleeding, heaviness, pruritus, and mucosal discharge after the Milligan-Morgan open haemorrhoidectomy in a randomized, observer-blinded, placebo-controlled clinical trial.

MATERIALS AND METHODS

Study design

Protocol synopsis for this trial and supporting CONSORT checklist were used as supporting information
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(Figure 1). Diosmin clinical trial was a phase II randomized, prospective, observer-blinded, placebo-controlled clinical trial.

**Inclusion/exclusion criteria**

Patients aged 12-75 years with an indication for haemorrhoidectomy were eligible for the study, provided that they met the following inclusion criteria: symptomatic and prolapsing hemorrhoids Grade III or IV and informed consent. Patients complicated with fistula or anal fissure, inflammatory bowel disease, dermatitis, proctitis, pregnancy or severe cardiovascular state or pulmonary complication were excluded from the study.

| Table 1 | Demographic data in Diosmin and control groups |
| --- | --- |
| | Diosmin groupa (n = 43) | Control groupb (n = 43) | P value |
| Mean age (yr) | 53.2 (11.2) | 51.3 (10.4) | 0.6332 |
| Male/female ratio | 26/17 | 24/19 | 0.6620 |
| No. of resected hemorrhoids | 3.4 ± 0.4 | 3.8 ± 0.5 | 0.1522 |
| Grades III/IV hemorrhoids | 33/10 | 29/14 | 0.9247 |
| Mean duration of hemorrhoidal disease (mo) | 21.6 (12.6) | 22.8 (14.5) | 0.6821 |
| Operating time (min) | 15.8 (1.9) | 16.9 (1.5) | 0.1295 |
| No. of constipation | 28 | 26 | 0.8235 |

1Patients treated with Diosmin; 2 Patients treated with placebo drug.

**Patients**

The study was conducted using a computer-randomized design. A total of 86 consecutive patients with the grades III and IV acute mixed hemorrhoids admitted to Anorectal Surgical Department of First Affiliated Hospital, Xinjiang Medical University from April 2009 to April 2010, were enrolled in this study. Demographic data (age and gender), disease grades, preoperative constipation status, mean duration of disease, operating time and number of resected piles were recorded for each patient. There were no statistical differences between the two groups in these aspects (Table 1).

**Medical and research ethics**

The trial was conducted in accordance with the principles of the Declaration of Helsinki19, the Guidelines for Good Clinical Practice (GCP) for Trials on Pharmaceutical Products20. The study protocol was approved by China governmental law and local regulations of Xinjiang Uygur Autonomous Region. This study was also conducted according to a protocol approved by the Medical Ethics Committee of First Affiliated Hospital of Xinjiang Medical University. Informed consent was obtained from all the patients or their relatives before the trial. The whole study consisted of two periods of observation (4 wk for each period). The last visit should be terminated in 90 d after operation.
Formal written informed consent was obtained from each patient after the preliminary assessment of patient's detailed history of the disease and general and systemic examination. The patients were subjected to a few baseline investigations (haemoglobin, bleeding time, clotting time, urine complete examination). They were randomly subjected to Diosmin or placebo depending on their choice, after discussing the advantages and disadvantages of both drugs with them. The study was “blind” and the observers evaluating the complication symptom parameters were unaware of the individual treatment schedules. Blinding and coding of the drugs were done by an independent monitor who was not an investigator after repackaging the look-alike capsules by a pharmaceutical company in Xinjiang. The codes were broken only after completion of the study.

**Surgery**

Two fixed anorectal surgeons performed all the procedures with the patient in the supine lithotomy position or jackknife position. All patients underwent proctoscopy in order to exclude other diseases in the rectum before surgery. The operations were carried out under spinal anesthesia with 15 mL bupivacaine with 1:200 000 adrenalin. Further 5 mL of the same solution was used to dissect the haemorrhoidal nodules from the internal sphincter. Except 3 patients, who had a considerable rectal mucosal prolapse and were treated with stapled haemorrhoidopexy, all the patients underwent the standard Milligan-Morgan haemorrhoidectomy.

We removed the haemorrhoidal nodule using an upside-down V-shaped incision on the anal dermis, without widening the surgical wound while approaching the sphincters. This was done in order to maintain ample mucous membrane bridges. Possible secondary nodules were removed through submucosa. Ligature of the vascular pedicle was performed clear of the internal sphincter. The extent of surgical incision was tailored according to the number of haemorrhoidal complexes. Hemorrhoids were excised to the anorectal junction or dentate line. The Milligan-Morgan open haemorrhoidectomy was performed by a standardized diathermy excision method. Diosmin was started on the 6th day after surgery. A standardized questionnaire was completed which included postoperative information about pain, bleeding, heaviness, pruritus, wound edema and mucosal discharge. The evolution of these symptoms during the postoperative period was assessed by means of patient’s self-questionnaires. Two predominant observatory parameters were postoperative pain and bleeding. Pain was assessed using verbal response scales and visual analog scale at hours 6 and 12 and on days 1, 2, 7 and 14 after operation. The verbal response scales had four options: no pain, mild pain, moderate pain, and severe pain. The visual analogue scale consisted of a 10-cm line with the words “no pain” on the left hand side and “worst pain imaginable” on the right. Two types of pain were assessed, pain on defecation and pain during the preceding 24 h. The scales for pain on defecation were completed immediately after defecation and the scales for 24 h pain completed each evening. In order that pain could be assessed for seven postoperative days, patients were asked to complete the forms at hospital. The use of narcotic drugs, antibiotics and laxatives, complication symptoms and hospital stay in all the patients were recorded after surgery. At the conclusion of the study, the codes were broken and the results were analyzed. The visual analogue scores were measured in cm, and the score for each 24 h was a single value. The score for pain on defecation was the mean value of scores during that day.

**Diosmin treatment**

All patients were routinely discharged on the first postoperative day unless otherwise clinically indicated. Eighty-six patients each were either given Diosmin 500 mg or received placebo medication according to the computer-randomized result. Diosmin 500 mg was given at a dose of 3 tablets twice daily, after meals, for 3 d followed by 2 tablets twice daily from day 4 to day 7. Each complication symptom was recorded at hours 6 and 12 and on days 1, 2, 7 and 14 after operation. On the 7th day, the symptoms and any relief were recorded and the dose was further reduced to one tablet twice daily for the next 15 d. Consequently follow-ups were made on days 15, 30 and 90.

**Assessment of postoperative symptoms**

The Milligan-Morgan open haemorrhoidectomy was performed by a standardized diathermy excision method. Assessment of postoperative symptoms was done in order that pain could be assessed for seven postoperative days, patients were asked to complete the forms at hospital, and any relief were recorded and the dose was further reduced to one tablet twice daily for the next 15 d. Consequently follow-ups were made on days 15, 30 and 90.

**Randomization**

Computer-based sequential method was used for the randomization at the completion of surgery into one of the two groups. This computer generated random codes used for envelopes containing the information “Diosmin” or “Placebo”. These envelopes were prepared by a statistician who was not involved the patient’s treatment or other work specific to the study. The computer randomization was completed in the Medical Statistical Center of Xinjiang Medical University.

**Statistical analysis**

Before initiating the trial, sample size was calculated us-
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Table 2 Postoperative course of Diosmin and control groups

|                      | Diosmin group¹ (n = 43) | Control group² (n = 43) | P value |
|----------------------|-------------------------|-------------------------|---------|
| Median hospital stay (d) | 6.1 (1.3)               | 7.3 (3.4)               | 0.0306  |
| Median time to first bowel action (h) | 48 (4.2)               | 56 (4.6)               | 0       |
| Median No. of bowel actions in the first week | 9 (2.3)               | 14 (3.1)               | 0       |

¹Patients treated with Diosmin; ²Patients treated with placebo drug. P value was the result of Mann-Whitney U test.

Table 3 Postoperative symptoms of Diosmin and control groups n (%)

|                      | Diosmin group¹ (n = 43) | Control group² (n = 43) | P value |
|----------------------|-------------------------|-------------------------|---------|
| Minor bleeding       |                         |                         |         |
| At 2 wk              | 3 (6.97)                | 11 (25.58)              | 0.0409  |
| At 8 wk              | 2 (4.65)                | 3 (4.64)                | 0.6449  |
| Heaviness            |                         |                         |         |
| At 2 wk              | 4 (9.30)                | 14 (32.56)              | 0.0171  |
| At 8 wk              | 2 (4.65)                | 8 (18.60)               | 0.0436  |
| Pruritus              |                         |                         |         |
| At 2 wk              | 9 (20.93)               | 18 (41.86)              | 0.0365  |
| At 8 wk              | 3 (6.97)                | 10 (23.25)              | 0.0351  |
| Mucosal discharge    |                         |                         |         |
| At 2 wk              | 7 (16.28)               | 11 (25.58)              | 0.2890  |
| At 8 wk              | 2 (4.64)                | 4 (9.30)                | 0.3972  |

¹Patients treated with Diosmin; ²Patients treated with placebo drug.

ing SPSS software 15.0 version. A power calculation estimated that 40 patients would be needed in each group to demonstrate a reduction of 20% pain with a power of 80% and at a 5% significance level. Discrete variables were analyzed using χ² test with Yates correction when appropriate. Continuous variables were analyzed by Wilcoxon signed tests for pared observations. Pain scores at each time interval were compared between groups with Wilcoxon’s rank-sum test (nonparametric analysis of ranked data). A two-tailed Spearman’s correlation coefficient was calculated where indicated. Statistical significance was assumed when P < 0.05. Statistical evaluation was done as intend-to-treat analysis. When not otherwise specified, data were presented as median and range.

RESULTS

After standard hemorrhoid surgery, 86 patients were allocated to receive Diosmin (experimental group, n = 43) and placebo capsules (control group, n = 43). None of the patients in either study group complained of any severe symptoms during the 90-d follow-up after treatment. The two groups were well matched for age, sex, disease grades, and number of piles. There were no statistical differences between the two groups in these aspects (Table 1).

The Diosmin group defecated earlier (P = 0.00), had more frequent bowel actions in the first postoperative week (P = 0.00), and had a shorter hospital stay (P = 0.03) compared with the placebo group (Table 2). No patient withdrew from the study because of any complaints. Significantly more placebo patients were troubled by minor rectal bleeding at 2 wk, although these rates were similar at 8 wk. The follow-up after 8 wk found that two patients experienced minor bleeding in Diosmin group, and therefore, underwent surgery. There was a statistically significant (P < 0.05) improvement in pruritus and heaviness at both 2 and 8 wk (Table 3). In addition, there was no statistical difference between the two groups in terms of wound mucosal discharge.

Patients in Diosmin group experienced significantly less pain at 6 and 12 h after surgery (P = 0.03, P < 0.01), and on days 1, 2, 7, 10, and 14 (P = 0.02, P < 0.01, P = 0.02, P = 0.03, P < 0.01) (Figure 2). There was also significant (P < 0.001) improvement on the proctoscopic appearance. Patients in the experimental group had significantly less defecation pain compared with the placebo group on days 1, 2, 7, 10, 14, and 30 (P = 0.03, P < 0.01, P < 0.01, P = 0.02, P = 0.04, P = 0.04) (Figure 3). No significant Diosmin-related complications or allergic reactions were reported by any patient. A similar number of patients reported burning with both treatments at the 2nd week after surgery (3 in Diosmin and 2 in placebo).

DISCUSSION

Haemorrhoid is a common disease affecting people of
all ages and both sexes. It is estimated that 50% of the people older than 50 years have hemorrhoid symptoms at least for a period of time. The causes of haemorrhoidal disease are multiple, but most are attributable to difficult passage of stool or constipation. Over the last few years, there has been increasing attention on surgical procedures to treat haemorrhoids. Several comparative studies have been performed to evaluate the available procedures to treat grades II, III, and IV hemorrhoids, and new surgical techniques, such as haemorrhoidectomy with Harmonic scalpel,[21,22] and Ligasure(TM)[23], Doppler-guided haemorrhoidal plexus ligation[24,25] and the stapled haemorrhoidopexy[26,27]. The most recent medium- and long-term studies on ample case series provide data on the efficacy, the results and complications of these techniques[28-30]. None of them proved to reduce complications such as pain and bleeding[21]. The ideal method should combine the high safety and efficacy of the treatment, yielding low postoperative pain and bringing comfort to the patients. Such considerations are related to the severity of the disease and can be addressed by evidence-based medicine by randomized, controlled trial. According to a recent meta-analysis of the Cochrane library[31], conventional haemorrhoidectomy as first described by Milligan and Morgan, is still the most widely used, effective, and definite surgical treatment for patients with symptomatic grades III and IV hemorrhoids. However, it is associated with significant postoperative complications such as pain, bleeding and mucous discharge. Although there is a consensus on the treatment of grades III and IV hemorrhoids, there is still confusion regarding the ideal treatment for these complications after surgery.

In 1971, Daflon, consisting of 90% Diosmin and 10% Hesperidin (Daflon 500; Serdia Pharmaceuticals, India and Vinosmin; Elder Pharmaceuticals, India), was firstly introduced in France by Bensaude et al[32] for the treatment of haemorrhoids and other capil Tulsa diseases. Diosmin mainly works on the inflammatory pathology of haemorrhoids by increasing the contraction of veins and local lymphatic drainage and decreasing the synthesis of prostaglandins such as PGE2 and thromboxane B2[33,34]. The anti-inflammatory effects of Diosmin are reflected in the reduction of capillary hyperpermeability and fragility in controlled clinical studies. Damom et al[35] found the same effects of Diosmin in increasing the duration of vascular contraction and prostaglandin components which are responsible for the inflammatory process. Diosmin also increases the local lymphatic drainage. Side-effects of the drugs are limited according to Meyer[36] who was first used Diosmin to treat hemorrhoid symptoms. He reported mild gastrointestinal and autonomic disturbances in 10% cases. A fixed micronized combination of the citrus bioflavonoids Diosmin (90%) and hesperidin (10%) has been widely used in Europe to treat diseases of the blood vessels and lymphatic system since 2000. The combination also appears to be beneficial for chronic venous insufficiency and venous stasis ulcers. Extensive safety evaluations have found that Diosmin/hesperidin was free from toxicological risk. From 2005, Diosmin was used to treat vascular diseases[40-48]. The obtained evidence strongly supports its use in hemorrhoids in recent years although only several randomized controlled trials were available.

In this randomized trial, we concluded that Diosmin leads to the rapid cessation of haemorrhoidal bleeding, alleviation of the associated symptoms and gives objective relief from complications of post-haemorrhoidectomy. This result is similar to Mlakar’s study[49]. In their study, Flavonoids was found very effective in the first 30 d of treatment and led to the rapid relief of various associated symptoms of haemorrhoid surgery. Because, up to now, there have only a few randomized controlled studies to investigate the effectiveness and safety of Diosmin to treat symptoms after haemorrhoidectomy in the world, we could not perform meta-analysis for these studies. In our study, Diosmin was more effective to control postoperative pain than placebo capsules during the early phase of the surgery. This is a highlight in our study. The Diosmin group defected earlier (P < 0.05), had more frequent bowel actions in the first postoperative week (P < 0.05), and had a shorter hospital stay (P < 0.05) compared with the placebo group. This is and a striking result compared with Mlakar’s study[49]. In spite of some minor bleeding, no patient withdrew from the study because of any kind of adverse events. This may be associated with proper drug usage after surgery, especially in the early phases. Significantly more placebo patients were troubled by minor rectal bleeding at 2 wk, although these rates were similar at 8 wk. However, during the follow-up after 8 wk, we found that two patients had minor bleeding in experimental group, therefore, they underwent surgery. Postoperative bleeding is a particularly important complication in hemorrhoids treatment due to its frequency varying between 0.6% and 10%(35,36). Sometimes bleeding may be alarming, because it may cause anemia very rapidly in the patients. Several randomized controlled studies evaluated the use of oral micronized, purified flavonoid fraction in the treatment of haemorrhoidal bleeding. In these studies, bleeding was relieved rapidly, and no complication was reported. This is somewhat conflict with our bleeding cases. However, we used 500 mg Diosmin capsules compared with 450 mg micronized purified flavonoid fraction in Yo YH’s study[48]. The most important reason of our poor result related with bleeding is that we included grades III and IV piles, but Yo YH’s study included only grades I, II, and III piles. A similar study of 100 patients reported that acute bleeding had subsided by the third day of treatment in 80% of patients receiving micronized flavonoids, 2 d sooner than in patients receiving a placebo. But, the different points compared with our trial, which were also disadvantages of their studies, were associated with the difference of their study designs. They compared micronized flavonoids medication with hemorrhoid surgery itself. Although we think Milligan-Morgan open haemorrhoidectomy is the most widely practiced “gold standard” surgical approach and the stages III and IV are the clear indication for this procedure, it is not necessary to alter the
indication for hemorrhoid surgery to medication. Another point is the cost of medication. A limitation of the drug is the lack of patient compliance due to the long duration of treatment and the high cost of the drug. The safety of the drug has already been proved but more studies need to be done to see if the total dose of Diosmin can be increased so as to increase the response rate and decrease the duration of postoperative treatment. A decrease in the cost of the drug should also be considered.

Purified flavonoid fraction is a botanical extract from citrus. It exerts its effects on both diseased and intact vasculature, increasing vascular tone, lymphatic drainage, and capillary resistance; it is also assumed to have anti-inflammatory effects and promote wound healing. In another recent randomized controlled trial, postoperative use of micronized, purified flavonoid fraction, in combination with short-term routine antibiotic and anti-inflammatory therapy, reduced both the duration and extent of postoperative symptoms and wound bleeding after haemorrhoidectomy, compared with antibiotic and anti-inflammatory treatment alone[18].

Postoperative pain is the most important uncomfortable aspect which was also our predominant observational parameter. Post haemorrhoid pain is difficult to assess, though verbal response scales and visual analogue scales are recognized methods. Maxwell concluded that the t test is "very robust" when comparing differences between visual analogue scale scores[40], and we therefore used this method of analysis. On two occasions, the verbal response scale in pain was a day less than the visual analogue scale. This may be because the discrete verbal response scale is less sensitive than the continuous visual analogue scale. Another highlight in our study was that patients in Diosmin group experienced significantly less pain at hours 6 and 12 (P < 0.05), and on days 1, 2, 7, 10, and 14 after surgery (P < 0.05). At the same time, patients in the experimental group had significantly less defecation pain compared with placebo groups on days 1, 2, 7, 10, 14 and 30 after surgery (P < 0.05). The exact cause of pain after haemorrhoidectomy has not yet to be defined. Various factors believed to be responsible for the pain including incarceration of smooth muscle fibers and mucosa in the transfixated vascular pedicle, epithelial denudation of the anal canal, and spasm of the internal sphincter[1]. Another reason for pain could be the development of linear wounds extending up to the anorectal ring, which appear similar to those of a chronic anal fissure[14]. Postoperative pain was also associated with bacterial fibrinolysis and defecation stress[49]. In our study, postoperative pain in the placebo group can be explained by the traction of the nonsensitive sliding haemorrhoidal tissue at the highly sensitive anal skin. The diminished postoperative pain in the Diosmin group might be related to its capillary resistance and diminished tissue edema and anti-inflammatory process. There was significant difference in different postsurgical days and weeks. Based on these results, we suggested that Diosmin has a clear action against anorectal postoperative pain. Therefore, it should be considered initially for patients presenting with haemorrhoidal symptoms after surgery. In addition, there was also a significant improvement on the proctoscopic appearance (P < 0.001).

Although there was a statistically significant improvement in heaviness and pruritus from baseline to the 8th week postoperatively, however, there were no statistical differences between the two groups in terms of wound mucosal discharge (P < 0.05). Our hypothesis was that our nonabsorbable suture used for internal mucosa ligation is responsible for this poor result.

In a 12-wk study of 50 pregnant women suffering from acute hemorrhoids, micronized Diosmin/hesperidin therapy was reported to be a “safe, acceptable and effective” treatment, and 66% obtained relief from symptoms within 4 d[80]. However, we suggest not using Diosmin for pregnant women, considering Diosmin is a new alternative for hemorrhoids.

This study has shown that Diosmin can reduce the complications from haemorrhoidectomy, especially in the early phase. We therefore suggest that this regimen should be a part of the routine postoperative management of patients for haemorrhoidectomy.

In conclusion, Diosmin (flavonoid fraction) has shown to be effective in alleviating symptoms after haemorrhoidal surgery and improving the proctoscopic appearance. Therefore, it should be considered initially for patients presenting with haemorrhoidal symptoms after surgery. However, further prospective randomized trials and longer follow-up are needed to confirm the findings of this study and observe the side effects of this drug.

**COMMENTS**

**Background**

Over the past few years, there has been increasing attention on surgical procedures to treat haemorrhoids. The Milligan-Morgan haemorrhoidectomy is still a major surgical approach for haemorrhoids. This study was designed to evaluate the influence of Diosmin on reducing postoperative pain, bleeding, heaviness, pruritus, and mucosal discharge after the Milligan-Morgan open haemorrhoidectomy in a randomized, observer-blinded, placebo-controlled clinical trial.

**Research frontiers**

Phlebotropic activity, protective effect on the capillaries and the anti-inflammatory effect of Diosmin have been reported in several studies in recent years. More recent clinical studies showed that flavonoid fraction such as Dalfon (phlebotropic agent) can reduce postoperative pain, bleeding and heaviness after haemorrhoidectomy.

**Innovations and breakthroughs**

This clinical trial has confirmed that Diosmin (flavonoid fraction) can reduce postoperative pain, bleeding and heaviness after Milligan-Morgan open haemorrhoidectomy.

**Applications**

Diosmin (flavonoidic fraction) has shown to be effective in alleviating symptoms after haemorrhoidal surgery and improving the proctoscopic appearance. Therefore, it should be considered initially for patients presenting with haemorrhoidal symptoms after surgery. However, further prospective randomized trials and longer follow-up are needed to confirm the findings of this study and observe the side effects of this drug.

**Terminology**

Diosmin is derived from some plants or used as a high-quality active ingredient in vein improvement supplements. Diosmin reduces inflammation and increases duration of vascular contraction that contributes to hemorrhoids.
Peer review
The authors engagingly described a pathomechanism of anal pain after haemorrhoidectomy and Diosmin’s action. The article is worth publishing.

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