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Research Article

The Efficacy of Adding Daflon to the Conventional Treatment on the Improvement of Symptoms and Health Related Quality of Life in Patients with Acute Hemorrhoids: A Randomized Clinical Trial

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Received: September 30, 2019; **Published:** October 28, 2019

Abstract

Introduction: Patients with acute hemorrhoids are often treated through endoscopic and surgical procedures. However, some patients are complaining of postoperative symptom recurrence. It has been shown that the administration of hesperidin reduces the severity of bleeding and the rate of recurrence. However, the efficacy rate of the medical treatment is still in doubt. The aim of this study was to assess the efficacy of adding daflon to the conventional treatment on the improvement of symptoms and health related quality of life in patients with acute hemorrhoids.

Methods and Materials: Nighty four adult patients with acute hemorrhoids were randomly assigned into the two groups: group A (topical anti-Hemorrhoid and lifestyle modifications) and the group B (daflon 1500 mg twice in a day orally in the first four days and 1000 mg twice in a day for three days later, added to the conventional treatment). Demographic, clinical data, SF-12V1 Health (mental and physical) Survey questionnaire were reported at baseline and two weeks after treatment.

Results and Findings: Forty five and 43 patients in Group A and group B completed the study, respectively. No significant differences were seen between treatment groups regarding the demographic and clinical data.

The bleeding rate was significantly improved in group B (P = 0.045). The study showed significant difference in physical, general health scores and the mean total SF-12 score between two treatment groups after two weeks of treatment (p values = 0.039, 0.036 and, 0.046, respectively).

Conclusion: Adding daflon to the conventional treatments of acute hemorrhoid is safe and can improve symptoms such as bleeding and health related quality of life in the patients with hemorrhoids.

Keywords: *Daflon; Acute Hemorrhoids; Pain Score; Bleeding; SF-12V1 Health Survey Questionnaire*

Introduction

Hemorrhoids is one of the most common medical condition in general population. The term "hemorrhoids" is used to define painless rectal bleeding with or without prolapse during defecation [1]. Patients experience different symptoms in a wide spectrum from mild itching to acute severe pain but most patient have mild symptoms treated without any need to medical treatment. Straining constipation, pregnancy and higher socioeconomic status increase the prevalence of hemorrhoid among individuals. The prevalence rate is variable range between 4.4% in one study and up to 40% in other studies, as many people do not seek proper medical attention or wrongly attribute other anorectal issues as being due to hemorrhoids [2-4].

Hemorrhoids are classified into two groups according of anatomical expression: internal and external. External hemorrhoid exist in the one third of outer anal channel and is covered by skin. The clinical manifestation of external hemorrhoids is characterized by bleeding and acute pain due to thrombosis. Internal hemorrhoids are fibro vascular tissue that is lined by columnar epithelium. Internal hemorrhoids represent 4 grade of prolapse and painless bleeding [5].

Grade 1: not prolapsing during defecation, Grade 2: prolapsing during defecation but spontaneously return to its internal position, Grade 3: prolapsing and requires the patient to push it inside manually, Grade 4: prolapsed and not reducible [1,6].

Conservative treatment such as life style and diet modification is recommended for grade1 and 2 hemorrhoids. Vasoactive medication and easy defecation can prevent prolapse and blood discharge. However, grade 3 and 4 need invasive procedures and should go under surgery. These non-surgical techniques are sclerotherapy, bipolar diathermy, infra-red photocoagulation or cryosurgery and ligation [7]. The main issue for patients is the pain after intervention [8].

One of the most important factor in acute bleeding of hemorrhoids is blood stasis in hemorrhoid plexus (rectal venous plexus) [9]. Flavonoids inhibit bleeding by increasing venous tone, reduction of blood stasis and improving of lymphatic drainage [10].

Although prescription of Hesperidin (daflon 500 mg) can reduce the severity of bleeding and prevent its recurrence, the efficacy of flavonoids in treatment of hemorrhoid is not clarified [11,12].

Aim of the Study

In this study, we aimed to evaluate the efficacy of daflon in improving symptoms of patients with acute hemorrhoidal disease and determine the side effects of it before and after the intervention in a randomized controlled trial.

Materials and Methods

Patients and study design

This is a randomized clinical trial. This study was approved by the institutional review board of the Iran University of Medical Sciences under the code of IR.IUMS.FMD.REC.1397.246. Written informed consent was provided by patients before their participation in the study.

Adult patients with the age more than 18 years and the diagnosis of acute hemorrhoids complaints (presence of acute anal pain and/or bleeding) who were referred to the gastroenterology clinic at Rasoul-e-Akram Hospital, Tehran were included in this study.

The patients with history of previous anorectal or hemorrhoid surgery, hemorrhoid grade I and IV, lactation, pregnancy, medications such as anti-depressant and flavonoid drugs, severe systemic disease, hypertension, seizure, cancer, sleep disorders, allergy to daflon and who were non- cooperative were excluded.

Intervention

The study comprised of two different groups: and group A; who received anti-hemorrhoidal ointment, life style change and using Seitz bath). Group B; who received daflon (500 mg tablets) for one week; three tablets BID (twice a day) for first four days and after that two tablets BID for next three days combined with conventional treatments.

A total of 88 patients were randomly assigned to the treatment groups by a computer generated random table. Accordingly, 45 patients and 43 patients were included in the group A and B, respectively. The flowchart of the study is demonstrated in figure 1.

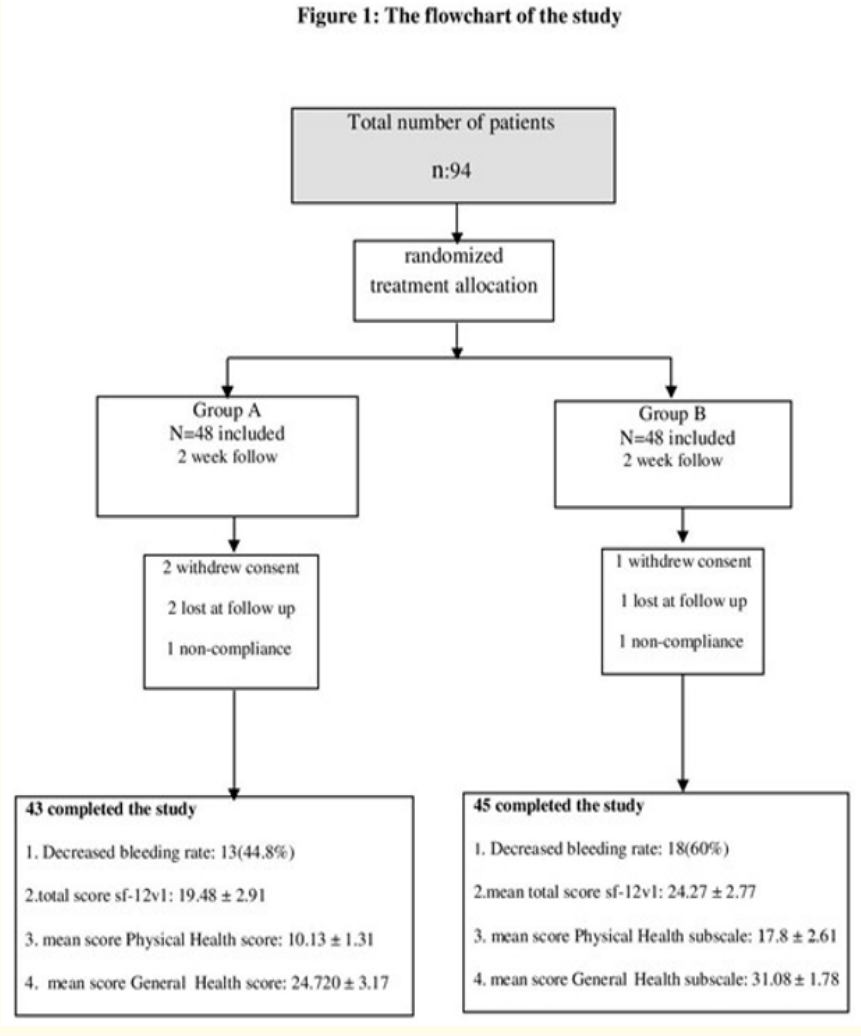

Figure 1: *The flowchart of the study.*

Outcome measures

Basic demographic and clinical data were recorded. Patients were followed for severity of pain, bleeding stopping rate and health status in two stages, before intervention and two weeks after starting the treatment. Also grade of hemorrhoid was gathered according to grading system mentioned earlier.

Severity of pain was measured using visual analogue scale (VAS). In this scale patients gave a score from 0 to 10, zero for no pain and 10 for the most pain they could imagine. The bleeding stopping rate was measured by these way, no bleeding, decreased bleeding,

un-changed bleeding. Three aspects of participants' health including physical health, mental health, general health and total scores were assessed with SF-12V1 Health Survey questionnaire. This questionnaire provided a score from 20 for physical health, from 27 for mental health and from 47 for general health. This questionnaires were completed over the in person visits. The physical component score (PCS) and mental component score (MCS) were also calculated using the norm-based scoring method [13]. The side effects of treatment and patients adherence to the treaments were investigated at the end of two weeks of treatment.

Sample size calculation

The sample size was calculated based on the mean difference of 15% for the percentage of satisfied patients from the study of Amato which compared the effect of daflon 500 mg in with a non- micronized diosmin [14]. With an effect size of 1.6 obtained from the difference of mean intestinal movements between the two study groups, at a power of 80% and significance level of 5%, a sample size of 50 patients in each group was regarded to be sufficient to detect a clinically important difference between the outcome measures of the study groups, using a One-way ANOVA test of the difference between means. It was assumed that the outcome measures are normally distributed.

Statistical analysis

SPSS for Windows version 16 was used for the statistical evaluations. Descriptive statistics were provided as the mean± standard deviation or number and percentage. Comparison of the mean between two groups was performed using independent t test for parametric and Mann–Whitney test for non-parametric variables. Chi-Square test was used to assess the relationship between the categorical variables. A P-value of less than 0.05 was considered statistically significant.

Results

A total of 88 patients completed the study that consisted of 43 patients in the group A and 45 patients in the group B. Thirty four (38.6%) of our patients were male with the mean age of 51.70 ± 13.96, ranging from 22 to 75 years. The mean disease duration was 40.66 ± 27.83 weeks ranging from 1 to 120 months. The mean of BMI was 24.11 ± 3.1 kg/m^2. Constipation was reported in 58 (66%), diarrhea in 14 (15.9%), normal bowel habits in 13 (14.7%) and mixed patterns of bowel habits in 3 (3.4%) patients. Hemorrhoid grade was the grade II in 75 (85.2%) patients, grade III in 13 (14.8%) patient. Bleeding status was the without bleeding in 30(34%), with each bowel movement in 21(23.8%), occasionally with bowel movement in 17(19.5%) and monthly in 20 (22.7%) patient.

No statistical difference was found between the basic characteristics of the case and control group (Table 1).

The basic total and subscale SF-12V1 Health Survey questionnaire scores of the two study groups were not significantly different at baseline.

Two weeks after the end of treatment, the mean total SF-12 score was 24.27 ± 2.77 in the group B and 19.48 ± 2.91in the group (p = 0.048). The mean of mental score was 16.6 ±2.4 in the group A and 71.3 ± 2.1 in the group B (p = 0.71). The physical role score was 10.13 ± 1.31 in group A and 17.8 ± 2.61in group B (p = 0.039). The general health score was 24.720 ± 3.17 in group A and 31.08 ± 1.78 group B (p = 0.036).

The mean pain score (VAS) was 4.23 ± 2.22 in the patients of group A and 4.32 ± 2.4 in the patients of group B. (p = 0.32). A significant difference was seen in decreased bleeding between two groups. (13(44.8%) and 18(60%) in group A and B, respectively. P = 0.042) (Table 2).

Mild and transient drug adverse effects were recorded in 4.4% (2/45) patients. Abdominal pain was the most common adverse reaction. The patient's adherence to treatment was excellent in both groups.

Discussion

Hemorrhoids is the most prevalent pathology of anorectal diseases which is characterized by prolapse and dilation of hemorrhoid plexuses. Hemorrhoids have a significant effect on quality of life. Most of the patients who suffer these complications can be treated by

Variable	Group A n = 43	Group B n = 45	P value
Age (year)	51.83 ± 13.28	50.64 ± 14.56	NS
BMI (kg/m^2)	24.53 ± 3.24	23.84 ± 3.11	NS
Disease duration (month)	37.16 ± 26.97	44.00 ± 28.53	NS
Sex			
Female	25 (58.1%)	29 (64.4%)	NS
Male	18 (41.9%)	16 (35.6%)	
Smoker	12 (27.9%)	12 (26.6%)	NS
Alcoholic	4 (9.4%)	5 (11.1%)	NS
Education level			
≤ Elementary	4 (9.4%)	2 (4.5%)	
Secondary school	31 (72%)	33 (73.3%)	NS
Academic education	8 (18.6%)	10 (22.2%)	
Marital status			
Married	31 (72%)	33 (73.3%)	NS
Not married	12 (28%)	12 (26.7%)	
Bowel status			
Diarrhea	8 (18.6%)	6 (13.3%)	
Constipation	26 (60.5%)	32 (71.1%)	NS
Normal	8 (18.6%)	5 (11.1%)	
Diarrhea and constipation	1 (2.3%)	2 (4.4%)	
Hemorrhoid grade			
Grade II	35 (81.4%)	40 (88.9%)	NS
Grade III	8 (18.6%)	5 (11.1%)	
Bleeding status			
Without bleeding	14 (32.7%)	15 (33.3%)	
With each bowel movement	10 (23.2%)	11 (24.4%)	NS
Occasionally with bowel movement	19 (44.1%)	19 (42.3%)	

Table 1: *The socioeconomic and demographic characteristics of patients in the treatment groups. NS: Non Significant; BMI: Body Mass Index.*

Variables		Group A n = 43 Mean ± SD	Group B n = 45 Mean ± SD	P value
Pain score (VAS)	Week 0	5.90 ± 1.55	6.06 ± 1.72	0.65
	Week 2	4.23 ± 2.22	4.32 ± 2.4	0.23
Bleeding score				
No bleeding	Week 2	1 (3.4%)	1 (3.3%)	0.089
Lower bleeding		13 (44.8%)	18 (60%)	0.042
Active bleeding		15 (51.7%)	11 (36.7%)	0.053
Physical Health	Week 0	11.09 ± 1.34	11.44 ± 2.31	0.22
	Week 2	10.13 ± 1.31	17.8 ± 2.61	0.039
Mental Health	Week 0	12.20 ± 2.66	12.02 ± 2.58	0.23
	Week 2	15.11 ± 1.452	16.28 ± 2.67	0.089
General Health	Week 0	22.69 ± 3.07	22.41 ± 3.81	0.073
	Week 2	24.720 ± 3.17	31.08 ± 1.78	0.036
Total score	Week 0	11.51± 2.82	11.11 ± 2.52	0.51
	Week 2	19.48 ± 2.91	24.27 ± 2.77	0.148

Table 2: *Comparison of the SF-12V1 Health Survey questionnaire total and sub-scales' score between the treatment groups.*

conservative medications. Patients with hemorrhoids treated successfully through invasive procedures but they complain of postoperative complications such as pain and bleeding [15-18].

The treatment of acute hemorrhoids is challenging for both the patients and physician. Here, we evaluated the efficacy of adding daflon to the conventional treatment on the improvement of symptoms and health related quality of life in the patients with acute hemorrhoids.

The average age of our patients was 50.62 ± 14.56 years but the different age categories was reported in previous studies [12]. We found that the disease was more common in females (64.4%) and the two third of the patients were housewives, as it was shown in previous studies [9].

The average range of BMI was about 27.70 ± 5.07 in this study. And there was a statistically significant occurrence of acute hemorrhoidal crisis in obese patients. Previous study demonstrated that major medical and socioeconomic issues could effect on the severity of acute hemorrhoid crisis, similar to our study [19].

Majority of our patients suffer from constipation and had pain in anal region. In addition, about half of the patients have defecation without bleeding and half of them have bleeding during every defecation. In this study 88.9% of patients have grade 2 of hemorrhoids as Meshikhes., *et al*. showed in 2004 [20,21].

In Participants' physical health and mental health Survey, there was no significant differences in mental health ($p = 0.298$) but from the point of physical health, there was a significant decrease ($p = 0.014$). We have not reported any deleterious adverse effects in this study, such as the previous studies [22].

The study of Diana., *et al*. in 2000 confirmed the efficacy of diosmin in reduction both of pain and blood, reducing 79% and 67%. The use of flavonoids seems to be effective in treatment of acute hemorrhoids crisis. Also Gianninni., *et al.* in 2015 demonstrate the significant effects of flavonoid mixture on the main issues of hemorrhoids crisis as we found. Furthermore, evaluation of pain before and after intervention showed that significantly decrease in them over time, in contrast to our study [23].

Past studies demonstrated that hesperidin (daflon) can reduce the severity of bleeding in acute hemorrhoids and prevent its recurrence, the efficacy of flavonoids in treatment of hemorrhoid is not clarified [11,12].

According to our results, two weeks after the end of treatment, the frequency of patients who experience lower bleeding per each bowel movement was significantly higher in the combination therapy group (group B). No significant differences regarding pain score was seen between treatment groups. All other SF-12v1 subscales scores, except for the mental health score, were significantly higher in the patient group B. The physical score were significantly improved by using combination therapy in group B ($p = 0.039$). No significant differences according to the mental health scores was seen between the treatment groups.

This study had some limitations. First of all, there was no specific scoring about bleeding stopping rate, as a major complaint in the patients with acute hemorrhoids. The second one was small sample size and short follow up duration. Third one was across the limited studies in this field.

Conclusion

Adding daflon to the conventional treatments of acute hemorrhoid crisis is safe and can significantly improve bleeding rate and physical and overall health related quality of life in these patients. Other studies should be designed to assess the role of daflon in medical and post-surgical maintenance therapy.

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Volume 6 Issue 11 November 2019