Efficacy of a standardized herbal preparation (Roidosanal®) in the treatment of hemorrhoids: A randomized, controlled, open-label multicentre study

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ABSTRACT

Background: Catechins and epicatechins are monomers of naturally occurring proanthocyanidins, which have been reported with free radical scavenging, antioxidant, antiinflammatory, antiallergic, and vasodilatory properties. Plant parts rich in proanthocyanidins have been used for years in treatment of various ano-rectal diseases. This study compares the efficacy of two herbal preparations, Daflon® 500 mg and Roidosanal®, in ameliorating the signs and symptoms associated with hemorrhoids. **Objective:** To evaluate the safety and to compare the efficacy of a herbal preparation, Roidosanal® versus Daflon® 500 mg, on signs and symptoms of hemorrhoidal disease. **Materials and Methods:** In this pilot, active controlled, open-labeled multicentre study, 73 patients with proctoscopy proven hemorrhoids (Grade I to III) were randomly assigned to receive either Roidosanal® (Gr R; *n* = 37) or Daflon® 500 mg (Gr D; *n* = 36), for 15 days, at three centers in India. Assessment of hemorrhoidal symptoms was carried out in all patients at different time points. Intent-to-treat analysis was performed for both primary and secondary endpoints. **Results:** Baseline characteristics were comparable between the two groups. Both products were found to be equally effective in improving the ano-rectal conditions in Grade I and Grade II hemorrhoids; however, Roidosanal® demonstrated better efficacy in patients with Grade III hemorrhoids. Hemorrhoids associated symptoms like bleeding, pain, etc., improved in both groups, although intergroup comparisons were comparable. **Conclusion:** Both Roidosanal® and Daflon® 500 mg were equally effective in resolving signs and symptoms of hemorrhoids. Roidosanal® can be tried as a safe and effective treatment option for treatment of hemorrhoids. Further randomized, double-blind and large multicentre studies are recommended.

Key words: Bleeding, catechins, flavonoids, hemorrhoids, proctoscopy

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Received: 26-Aug-2013
Revised: 28-Oct-2013
Accepted: 26-Jan-2014

Access this article online	
Quick Response Code:	Website: www.jaim.in
	DOI: 10.4103/0975-9476.131732

INTRODUCTION

Hemorrhoids are one of the most common gastrointestinal disorders seen by general practitioners. It has been estimated that they can occur at any age and can affect both men and women.[1] The natural evolution of hemorrhoids is benign in nature, but they tend to get worse over time, and therefore they should be treated as soon as it occurs. The term hemorrhoids (or piles) is used to describe the enlargement of the venous tissues of the anal region, which becomes inflamed or prolapsed.[2]

The anal canal consists of three fibrovascular cushions that are supported within the anal canal by a connective tissue framework, which is important in providing a watertight

seal to the anus. Hemorrhoids result from the hypertrophy of the hemorrhoidal plexus and pathological changes in the anal cushions.[3,4] The degenerative effects of aging and regular straining during bowel movements may weaken the supporting tissues, producing a shearing force on the cushions, causing their descent and prolapse. The prolapsed cushions impair venous return, resulting in engorgement that may be further exacerbated by chronic straining during defecation, inadequate fiber intake, and conditions such as pregnancy, that raise intraabdominal pressure. Bleeding from the engorged prolapsed hemorrhoid occurs as a result of localized mucosal trauma or inflammation, which damages the underlying blood vessels. The anal cushions of patients with hemorrhoids show significant pathological changes like abnormal venous dilatation, vascular thrombosis, degenerative process in the collagen fibers and fibroelastic tissues, distortion and rupture of the anal subepithelial muscle.[5] The symptoms associated with hemorrhoids include rectal bleeding, perianal pain, discomfort, mucous discharge, perianal itching, and irritation.[3,4,6-8]

Hemorrhoids are generally classified according to their position relative to the dentate line. External hemorrhoids originate below this line and become symptomatic only when thrombosed. Internal hemorrhoids arise above the dentate line and are marked by bleeding and protrusion.[9] They can be further graded according to the degree of prolapse.[10,11] Internal hemorrhoids that bleed but do not prolapse are designated as Grade I hemorrhoids; those that prolapse and reduce spontaneously (with or without bleeding) are second grade hemorrhoids; prolapsed hemorrhoids requiring manual reduction are Grade III hemorrhoids; and prolapsed hemorrhoids that cannot be reduced are Grade IV hemorrhoids.

Treatment options vary based on the degree and severity of symptoms. Management of hemorrhoids may be medical (prescribing high fiber diet, antimotility agents, topical analgesics and corticosteroid creams for symptomatic relief, alternative/traditional medicine like oral flavonoids), nonoperative (sclerotherapy, cryotherapy, rubber band ligation, infrared photocoagulation, etc.) or surgical (open, closed, or stapled hemorrhoidectomy). In many countries, 70-80% of the population use traditional medicine for primary health care. As per World Health Organization (WHO), 80% of about 4000 million inhabitants on this planet rely on plant medicines.[12] Traditional healthcare systems are known to have different treatment regimens for management of hemorrhoids. Ayurveda is one of the traditional health care systems prevalent and practiced widely in India and other countries. Indian Regulations permit use of traditional medicine under proprietary ayurvedic medicine licenses. The preparations are approved by the state regulatory bodies and marketed. Several qualified ayurvedic physicians (~*Vaidyas*) practice traditional methods and use traditional medications for management of hemorrhoids. There are over half a million ayurvedic practitioners and over 800,000 registered traditional medicine practitioners in India.[13]

Proanthocyanidins, present in various plant parts, comprising of catechins and epicatechins, have been reported with free radical scavenging, antioxidant,[14-18] antiinflammatory, antiallergic, and vasodilatory activity.[19,20] Proanthocyanidins have been shown to inhibit the enzymes hyaluronidase, elastase, and collagenase, which degrade connective tissue structures leading to increased vascular permeability.[21,22] Moreover low compliance associated with treatments such as diet and lifestyle changes, hydrotherapy and mechanical compression therapy, renders oral therapy as an attractive option.[15] Several studies have assessed the use of oral micronized, purified flavonoid fraction (MPFF) (Daflon® 500 mg),[23-27] and is one of the most commonly used treatment option for Grade 1 and Grade II hemorrhoids.[28]

On the basis of above considerations and probable mechanisms of action, we planned to use a marketed herbal preparation, Roidosanal® (as capsules; standardized to contain not less than 7% of total catechins and epicatechins). Both the above products possess similar active chemical entities (flavonoids) and therefore assumed to have a similar mechanism of action. We conducted a pilot scale, open-labeled, multicentre study to determine the safety of Roidosanal® capsules, and to compare its efficacy against Daflon® 500 mg, in patients with hemorrhoids.

MATERIALS AND METHODS

Study design

This study was a multicentric, randomized, open labeled study conducted at three centers, namely, Mohinder Hospital, Batra Hospital and Research Center, and South End Clinic, in New Delhi from January 2009 to June 2010. The study was approved by an independent ethics committee. The study project was supported by Next Gen Pharma India Pvt. Ltd., New Delhi, India.

Participants

Patients of either gender, aged ≥18 years, with hemorrhoids confirmed by proctoscopy, visiting the recruitment centers were enrolled in the study. All patients had given signed informed consent before examination. Any patient presenting with anal fissures along with hemorrhoids was also recruited. Patients diagnosed with bleeding hemorrhoids and having no other abnormal vital signs and symptoms were included in the study. Pregnant and lactating women, alcoholics, and

patients currently using other antihemorrhoidal drugs or planning to undergo any surgical procedure for hemorrhoids were excluded from the study.

Intervention

The test product consisted of a processed herbal preparation, Roidosanal® (By Next Gen Pharma India Pvt. Ltd.) and it was compared with Daflon® 500 mg (By Serdia Pharmaceuticals (India) Pvt. Ltd.). Roidosanal® is a processed preparation from a mixture of four herbs, that is, gum-resin from *Commiphora molmol* (50%), gum-resin from *Gardenia* spp. (16.6%) and inflorescence from *Tagates erecta* (16.7%), and *Mesua ferrea* (16.7%). It is formulated as capsules and standardized to contain not less than 7% of total catechins and epicatechins. The control preparation, Daflon® 500 mg contains micronized purified flavonoid extracts of rutaceae 500 mg, equivalent to 450 mg of diosmin, and 50 mg of hesperidine per tablet. Daflon® 500 mg is marketed in India for treatment of venous diseases, namely, chronic organic and functional venous deficiency of lower limbs, varicose veins, sequelae of phlebitis, hemorrhoids, etc.[23] Test product and comparator for the study were supplied by the sponsor. Patients were randomized at the initial consultation visit to receive either of the two treatments, Roidosanal® Caps (2 caps twice daily; Gr R) or Daflon® 500 mg Tabs (2 tablets daily; as per the recommended dosage in package insert of the product; Gr D), for 15 days. Compliance was ensured by project staff through regular phone calls and pill count at the end of treatment regimen. Patients were advised to restrict the amount of salt and spices in food. No laxatives or use of any other antihemorrhoidal drugs were allowed during the trial period.

Adverse events

All observed and reported adverse events regardless of treatment group or suspected causal relationship were recorded on the adverse events page of the case report proforma. Abnormal findings and clinically significant changes such as excessive pain and bleeding, abnormal local pain or itching were evaluated during clinical and physical examination.

Randomization and allocation concealment

Randomization was performed using permuted blocks of ten. The randomization list and numbered packing of intervention was carried out by a person not involved in the study. All the interventions and random numbers were packed in separate opaque envelopes. The interventions were dispensed in a serial fashion to the patients.

Study assessments

On visit 1, screening and randomization was done. This involved signed informed consent and enrolment of patients as per the inclusion and exclusion criteria. Demographics and medical history including previous history of hemorrhoids or any other chronic diseases was assessed. Proctologic examination was performed to assess the hemorrhoidal conditions, and then the patients were randomized. The investigational products were given to all patients for 15 days with instructions for administration. Each patient's condition was assessed telephonically on the 8th day. On visit 2 (day 16) proctological examination was conducted again and it marked the end of treatment. However, the patients were followed-up, with visit 3 being the last visit, at the end of day 45. Tolerability of the interventions was evaluated subjectively by the investigator. Details of assessments done at each visit are explained below.

Proctoscopy was performed at baseline and end of treatment (16th day) by the same proctoscopy surgeon. Proctologic assessment was performed in the left-lateral position by inspection of the anal verge of the anal canal by using a proctoscope.[29,30] Parameters namely, grade (I, II, III, IV) and position of hemorrhoids (at one site, two sites or all three primary sites, i.e., 3'O clock, 7'O clock, 11'O clock position) were assessed. Hemoglobin and fecal occult blood tests were performed at baseline, 16th, and 45th day. Parameters namely, bleeding, itching, soiling, tenesmus, constipation, irritation after defecation per rectum were assessed qualitatively as Yes/No and frequency was measured quantitatively as none/week, 1-2 times/week or more than 2 times/week, at baseline, 8th, 16th, and 45th day of study. Anal pain was also recorded at the same time points using a linear visual analogue pain score (VAS) (range 0-10, 0 = no pain and 10 = the worst possible pain). However, the VAS score was regrouped as 1-3 = mild pain, 4-6 = moderate, and 7-10 = severe pain.[31]

Endpoints

The primary end points included change in "Grade" and "Position" of hemorrhoids, as measured using a proctoscope. Secondary end points included changes in hemorrhoidal signs and symptoms namely, bleeding, itching, pain, soiling, tenesmus, irritation after defecation, and constipation.

Sample size calculation and statistical assessment

Since this was the first randomized study using Roidosanal®, a pilot study was designed and therefore, sample size calculation was not done.

Mean ± standard deviation was computed for continuous variables. Frequencies and percentages were calculated for categorical data of all symptoms. Bivariate relationships between pair of variables were analyzed using Fisher's exact test and Chi-square test. The analysis was subjected further

to intention-to-treat analysis. Analysis was performed for all the primary and secondary end points. For the purpose of analysis, patients who dropped out before the 45-day time point, their data were carried forward from their last assessment to be included in the final analysis. A *P* value of 0.05 or less was considered statistically significant and that of 0.001 or less was considered highly statistically significant. The data were analyzed by using SPSS statistical software version 16.0 (Statistical Package for Social Sciences; SPSS Inc, Chicago, IL).

RESULTS

One hundred and twenty patients were screened, of whom 28 patients were excluded as they did not fulfill selection criteria and 19 patients voluntarily declined to be a part of the study. Out of 73 randomized patients, 37 patients (28:9 = Male: Female) received Roidosanal®(Gr R) and 36 patients (29:7 = M: F) received Daflon® 500 mg (Gr D) in a controlled fashion as shown in Figure 1. The mean age of patients in Gr R and Gr D was 36 and 32 years, respectively. A total of 73% in Gr R and 81% patients in Gr D had no history of pelvic surgery before the treatment. About 71% and 84% patients in Gr R and Gr D respectively, had no history of usage of medications for hemorrhoids. There were no significant differences in baseline characteristics for age, gender, past history of hemorrhoids, and duration of hemorrhoids and with regard to other ano-rectal disorders, grade of hemorrhoids, pain, bleeding, itching, soiling, irritation after defecation, constipation, tenesmus, and hemoglobin. Patients were allocated in a controlled fashion, keeping the randomization unbiased. Twenty-two (59.5%) patients in Gr R and 15 (41.7%) patients in Gr D completed the study. No serious adverse events were reported with either of the two treatment regimens, gastrointestinal upset was observed in three patients in Gr D.

Response in ano-rectal conditions

The distribution of patients at baseline between the two groups in terms of ano-rectal conditions were comparable ($P = 0.299$; Table 1). Both Roidosanal® ($P < 0.001$) and Daflon® 500 mg ($P = 0.027$) significantly improved the ano-rectal conditions [Table 1].

Severity of hemorrhoids (grade and position of hemorrhoids)

The percentage distribution of all patients with regard to site and grade is shown in Table 1. Roidosanal® and Daflon® 500 mg were equally effective in patients with Grade I and Grade II hemorrhoids. Roidosanal® showed better efficacy and faster resolution of signs and symptoms in patients with Grade III hemorrhoids. A significantly higher number of patients with Grade III hemorrhoids improved in Gr R as compared with Gr D (six patients in Gr R vs 0 patients in Gr D; *P* value < 0.05; Binomial test; not shown in Table 1). This is an important aspect, as Grade III hemorrhoids, unlike Grade I and II hemorrhoids, do not usually present spontaneous improvement of the symptoms.

Symptoms associated with hemorrhoids

Bleeding

Intergroup analysis revealed that both Daflon® 500 mg and Roidosanal® were comparable in decreasing the extent and

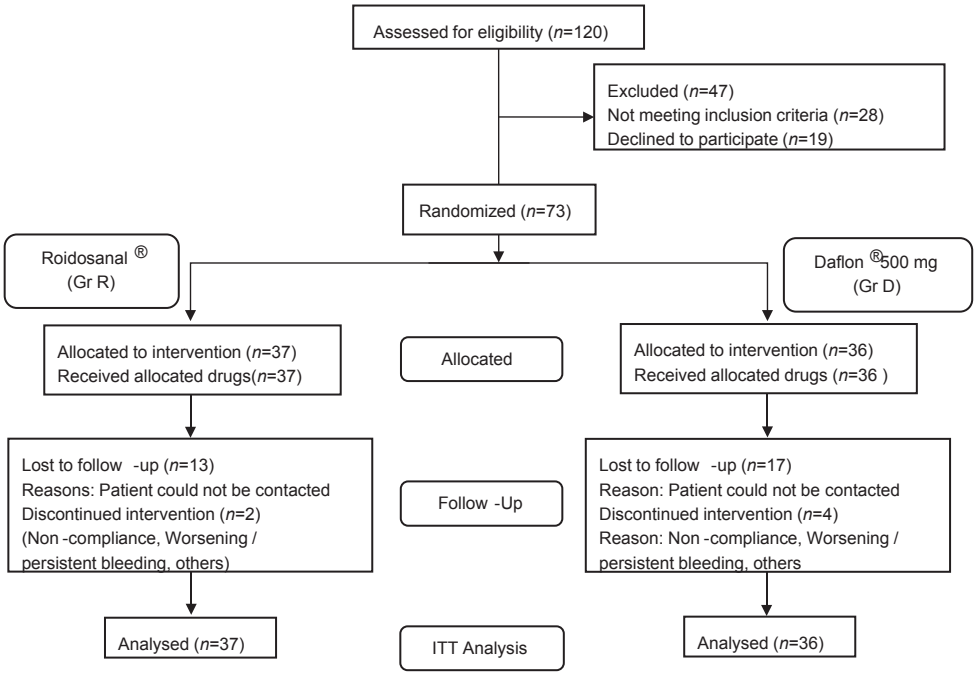

Figure 1: Flow of patients

frequency of bleeding associated with hemorrhoids at all visits. Intragroup analysis showed that there were lesser no. of patients in Gr R with complaints of bleeding as compared with patients in Gr D on Day 8 ($P = 0.004$ vs $P = 0.102$, Figure 2). The number of patients complaining of bleeding decreased in both groups on Days 16 and 45, but did not reach statistical significance. The frequency of bleeding [Table 3] decreased significantly in both groups on Day 8 ($P = 0.050$ and $P = 0.046$ in Gr R and Gr D respectively) as compared with baseline, however, the changes on Days 16 and 45 did not reach statistical significance. This could be due to a smaller sample size owing to a pilot trial design.

Pain

There was significant decrease in severity and frequency of ano-rectal pain in both groups on Days 8, 16, and 45 [Figure 3 and Table 3]. The intergroup analysis was comparable as both products demonstrated similar efficacy in relieving severity and frequency of pain on 8th, 16th, and 45th day [Figure 3 and Table 3].

Itching

Both Roidosanal® and Daflon® 500 mg were equally effective in relieving the itching symptom and reducing its frequency [Tables 2 and 3]. The relief from itching was observed as early as on the 8th day, lasting till the end of study. There was no significant difference in the efficacy of both products in relieving symptoms of itching, when compared against each other at all visits [Tables 2 and 3].

Soiling

Eight (21.6%) patients in Gr R and five (13.9%) patients in Gr D complained of soiling at baseline. However, both the products were able to provide relief from soiling immediately, and lasting till the end of treatment [Tables 2 and 3].

Tenesmus

Intergroup analysis did not yield any significant difference; both Roidosanal® and Daflon® 500 mg were equally effective in relieving tenesmus symptom. Both the treatments

Table 1: Ano-rectal conditions of patients at baseline and after treatment on day 16

Parameters	Gr R, *n* (%)			Gr D, *n* (%)			*P* value^ (Gr. R vs Gr. D)
	Baseline@	After treatment#	*P* value	Baseline@	After treatment#	*P* value	
Ano-rectal condition							
No active hemorrhoids	0 (0)	3 (8.1)	<0.001*	0 (0)	1 (2.8)	0.027*	ns*
Internal hemorrhoids	18 (48.6)	25 (67.6)		21 (58.4)	27 (75)		
Hemorrhoids with fissures	1 (2.8)	2 (5.4)		3 (8.3)	4 (11.1)		
Internal hemorrhoids and fissures	18 (48.6)	7 (18.9)		12 (33.3)	4 (11.1)		
Site of hemorrhoids							
One site	17 (53.1)	19 (59.4)	0.120*	13 (43.4)	16 (53.3)	<0.001*	ns*
Two sites	11 (34.4)	11 (34.4)		11 (36.6)	9 (30)		
All three sites	4 (12.5)	2 (6.2)		6 (20)	5 (16.7)		
Grades of hemorrhoids							
Grade I	6 (18.7)	8 (25)	0.023*	7 (23.3)	10 (33.3)	<0.001*	ns*
Grade II	15 (46.9)	19 (59.4)		16 (53.4)	12 (40)		
Grade III	11 (34.4)	5 (15.6)		7 (23.3)	8 (26.7)		

@Beginning of treatment (Day 1); #End of treatment (Day 16); ^*P* values for comparison between groups after treatment; *Pearson Chi-square test; ns=Not significant. Distribution of patients at baseline: Gr. R vs Gr D (P =0.299, Pearson Chi-square test)

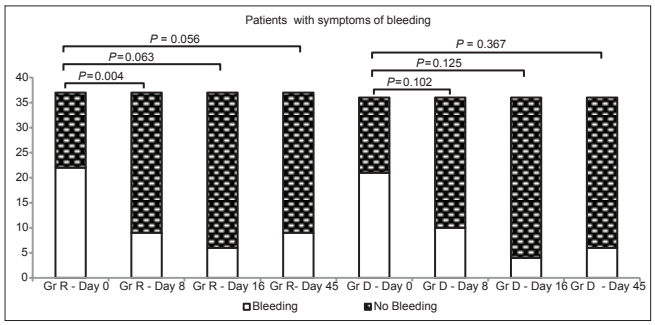

Figure 2: Distribution of patients with bleeding symptom at baseline and at follow-ups. Within group differences as depicted above were compared using Pearson chi-square test. Between group differences (Roidosanal® vs Daflon®) at all visits were comparable (Pearson chi-square test; Day 0, $P = 0.922$; Day 8, $P = 0.737$; Day 16, $P = 0.526$; Day 45, $P = 0.418$)

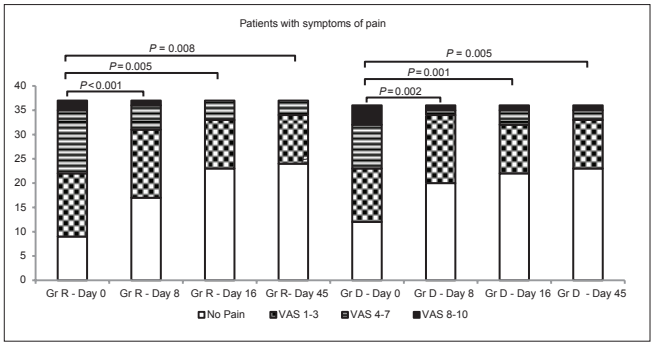

Figure 3: Distribution of patients with pain symptom at baseline and at follow-ups. Within group differences as depicted above were compared using Pearson chi-square test. Between group differences (Roidosanal® vs Daflon® at all visits were comparable (Pearson chi-square test; Day 0, $P = 0.577$; Day 8, $P = 0.408$; Day 16, $P = 0.765$; Day 45, $P = 0.751$)

Table 2: Hemorrhoidal symptoms at baseline and outcome on days 8, 16 and 45

Presence of symptoms	Gr R, *n* (%)				Gr D, *n* (%)				Gr R vs Gr D		
	Day 0	Day 8	Day 16	Day 45	Day 0	Day 8	Day 16	Day 45	*P* value#	*P* value*	*P* value+
Itching											
Yes	20 (54.1)	12 (32.4)	12 (32.4)	12 (32.4)	17 (47.2)	10 (27.8)	12 (33.3)	9 (25.0)	0.559	0.935	0.483
No	17 (45.9)	25 (67.6)	25 (67.6)	25 (67.6)	19 (52.8)	26 (72.2)	24 (66.7)	27 (75)			
P value		0.001$^{\alpha}$	0.001$^{\beta}$	0.013$^{\delta}$		<0.001$^{\alpha}$	<0.001$^{\beta}$	0.004$^{\delta}$			
Soiling											
Yes	8 (21.6)	4 (10.8)	3 (8.1)	2 (5.4)	5 (13.9)	1 (2.8)	0 (0)	0 (0)	0.388	0.240	0.493
No	29 (78.4)	33 (89.2)	34 (91.9)	35 (94.6)	31 (86.1)	35 (97.2)	36 (100)	36 (100)			
P value		<0.001$^{\alpha}$	<0.001$^{\beta}$	0.006$^{\delta}$		0.012$^{\alpha}$	n.d.	n.d.			
Tenesmus											
Yes	16 (43.2)	7 (18.9)	6 (16.2)	4 (10.8)	16 (44.4)	12 (33.3)	7 (19.4)	4 (11.1)	0.918	0.719	0.999
No	21 (56.8)	30 (81.1)	31 (83.8)	33 (89.2)	20 (55.6)	24 (66.7)	29 (80.6)	32 (88.9)			
P value		0.012$^{\alpha}$	0.206$^{\beta}$	0.175$^{\delta}$		0.001$^{\alpha}$	0.109$^{\beta}$	0.018$^{\delta}$			
Irritation after defecation											
Yes	26 (70.3)	13 (35.1)	12 (32.4)	8 (21.6)	20 (55.6)	15 (41.7)	13 (36.1)	11 (30.6)	0.193	0.741	0.384
No	11 (29.7)	24 (64.9)	25 (67.6)	29 (78.4)	16 (44.4)	21 (58.3)	23 (63.9)	25 (69.4)			
P value		0.004$^{\alpha}$	0.006$^{\beta}$	0.038$^{\delta}$		<0.001$^{\alpha}$	0.001$^{\beta}$	0.005$^{\delta}$			
Constipation											
Yes	26 (70.3)	15 (40.5)	13 (35.1)	9 (24.3)	26 (72.2)	17 (47.2)	10 (27.8)	9 (25)	0.854	0.499	0.947
No	11 (29.7)	22 (59.5)	24 (64.9)	28 (75.7)	10 (27.8)	19 (52.8)	26 (72.2)	27 (75)			
P value		0.001$^{\alpha}$	0.004$^{\beta}$	0.025$^{\delta}$		0.042$^{\alpha}$	0.518$^{\beta}$	0.667$^{\delta}$			

$^{\alpha}$Comparison within group, Baseline vs Day 8; $^{\beta}$Comparison within group, Baseline vs Day 16; $^{\delta}$Comparison within group, Baseline vs Day 45; #Comparison between groups at Baseline; *Comparison between groups at Day 16; +Comparison between groups at Day 45; n.d.=Cannot be determined; Statistical test used: Pearson Chi-square test

Table 3: Frequency of hemorrhoidal symptoms at baseline and outcome on days 8, 16, and 45

Frequency of symptoms	Gr R, *n* (%)				Gr D, *n* (%)				Gr R vs Gr D		
	Baseline	Day 8	Day 16	Day 45	Baseline	Day 8	Day 16	Day 45	*P* value#	*P* value*	*P* value+
Bleeding											
None	15 (40.6)	28 (75.7)	31 (83.8)	28 (75.7)	15 (41.7)	26 (72.2)	32 (88.9)	30 (83.3)	0.56	0.367	0.59
1-2 times/week	6 (16.2)	7 (18.9)	4 (10.8)	6 (16.2)	9 (25.0)	4 (11.1)	1 (2.8)	3 (8.3)			
>2 times/week	16 (43.2)	2 (5.4)	2 (5.4)	3 (8.1)	12 (33.3)	6 (16.7)	3 (8.3)	3 (8.3)			
P value		0.050$^{\alpha}$	0.180$^{\beta}$	0.174$^{\delta}$		0.046$^{\alpha}$	0.061$^{\beta}$	0.150$^{\delta}$			
Pain											
None	9 (24.3)	17 (45.9)	23 (62.2)	24 (64.9)	12 (33.3)	20 (55.6)	23 (63.9)	24 (66.7)	0.665	0.974	0.974
1-2 times/week	6 (16.2)	12 (32.4)	6 (16.2)	8 (21.6)	6 (16.7)	8 (22.2)	6 (16.7)	7 (19.4)			
>2 times/week	22 (59.5)	8 (21.6)	8 (21.6)	5 (13.5)	18 (50.0)	8 (22.2)	7 (19.4)	5 (13.9)			
P value		0.001$^{\alpha}$	0.007$^{\beta}$	0.074$^{\delta}$		<0.001$^{\alpha}$	0.020$^{\beta}$	0.009$^{\delta}$			
Itching											
None	17 (45.9)	25 (67.6)	26 (70.3)	26 (70.3)	19 (52.8)	26 (72.2)	25 (69.4)	28 (77.8)	0.657	0.898	0.722
1-2 times/week	6 (16.2)	5 (13.5)	7 (18.9)	6 (16.2)	7 (19.4)	5 (13.9)	8 (22.2)	5 (13.9)			
>2 times/week	14 (37.8)	7 (18.9)	4 (10.8)	5 (13.5)	10 (27.8)	5 (13.9)	3 (8.3)	3 (8.3)			
P value		0.004$^{\alpha}$	0.023$^{\beta}$	0.037$^{\delta}$		< 0.001$^{\alpha}$	0.001$^{\beta}$	0.002$^{\delta}$			
Soiling											
None	29 (78.4)	33 (89.2)	34 (91.9)	35 (94.6)	31 (86.1)	35 (97.2)	36 (100)	36 (100)	0.239	0.218	0.493
1-2 times/week	3 (8.2)	2 (5.4)	2 (5.4)	2 (5.4)	4 (11.1)	1 (2.8)	0 (0)	0 (0)			
>2 times/week	5 (13.4)	2 (5.4)	1 (2.7)	0 (0)	1 (2.8)	0 (0)	0 (0)	0 (0)			
P value		< 0.001$^{\alpha}$	0.004$^{\beta}$	0.016$^{\delta}$		0.016$^{\alpha}$	n.d.	n.d.			

$^{\alpha}$Comparison within group, Baseline vs Day 8; $^{\beta}$Comparison within group, Baseline vs Day 16; $^{\delta}$Comparison within group, Baseline vs Day 45; #Comparison between groups at Baseline; *Comparison between groups at Day 16; +Comparison between groups at Day 45; n.d.=Cannot be determined; Statistical test used: Pearson Chi-square test

improved the symptoms of tenesmus significantly after 8 days of treatment [Table 2].

Irritation after defecation

Intergroup analysis revealed a similar efficacy of both treatments [Table 2]. Intragroup analysis demonstrated that patients in both groups were relieved of the irritation after defecation symptom on Days 8, 16, and 45 in a significant manner as compared with baseline [Table 2].

Constipation

Patients with history of constipation in Gr R were relieved significantly on 8th ($P = 0.001$), 16th ($P < 0.004$), and 45th Day ($P < 0.025$) as compared with baseline.

Patients in Gr D showed significant relief only on the 8th day ($P = 0.042$; Table 2). The relief with Roidosanal® was prompt, achieved within 8 days of treatment, and sustained till the end of treatment and follow-up visit.

Diarrhea

Two (5.4%) patients in Gr R and 1 (2.8%) patient in Gr D complained of diarrheal symptoms at baseline ($P = 0.999$). Diarrheal symptoms improved in two patients (one in Gr R and one in Gr D) after treatment.

Hemoglobin level

Mean hemoglobin level at baseline was found to be 12.52 and 12.54 g/dl in Gr R and Gr D, respectively. Hemoglobin levels slightly improved after treatment (12.69 g/dl in Gr R and 12.70 g/dl in Gr D); however, the change between the groups or within group was not significant.

DISCUSSION

Though there is anecdotal evidence demonstrating the use of herbal medicines containing bioflavonoids in ano-rectal diseases, scientific studies in this field are grossly inadequate. Herbal products are attracting attention in developed countries too, as an alternative to high cost modern drugs and associated side effects.

A comparative, open label trial in different grades of hemorrhoids, confirmed by proctoscopy was conducted in a total of 73 patients at three centers in urban and semi-urban areas catering to varied population of socioeconomic status and educational levels. The selected patients were randomly allocated to two groups, namely, a group taking processed herbal preparation (Roidosanal®) or a popularly prescribed preparation (Daflon® 500 mg) available in Indian market. The characteristic signs and symptoms of hemorrhoids were scored for both groups at baseline, 8th, 16th, and on 45th day of treatment.

Therapeutic objectives in treatment of piles include shrinkage of piles mass, subsiding inflammation and preventing infection in the anal region, preventing bleeding from the rectum, relieving itching in the anal region, and relieving constipation as well. Of all the above, reduction in inflammation, bleeding, and pain bring immediate relief to the patient, and is of considerable importance to the treating physician. The study results showed that the Roidosanal® was effective in ameliorating ano-rectal conditions and associated signs and symptoms of hemorrhoids. The current study, although with a limited sample size was able to demonstrate the superior efficacy of Roidosanal® over Daflon® 500 mg, in improving the ano-rectal symptoms in patients, particularly with Grade III hemorrhoids. Prompt resolution of bleeding symptom on the 8th day was also observed with Roidosanal®. Treatment with either therapies demonstrated a significant response in Grade I and Grade II hemorrhoids, bleeding, pain, anal itching, soiling, and constipation. The study also demonstrates the importance of traditional medicine in the normal routine of a patient with hemorrhoids unless there is an absolute need for surgical intervention.

Limitations of the study included a pilot design (no sample size calculation), open label design, and no central laboratory for biochemistry tests or proctoscopy.

CONCLUSION

Roidosanal® was found to be equally effective as Daflon® 500 mg in improving ano-rectal conditions and associated signs and symptoms of hemorrhoids. There were no major adverse events associated with the use of either product. Treatment of patients with Grade I to Grade III hemorrhoids with preparations like Roidosanal® or Daflon® 500 mg would be beneficial and can be looked for. Further large and double-blind trials with proper statistical methods need to be conducted to confirm the results.

ACKNOWLEDGMENT

The authors express their gratitude to Next Gen Pharma India (New Delhi) for the financial support and for providing the study medications used in the study.

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How to cite this article: Aggrawal K, Satija N, Dasgupta G, Dasgupta P, Nain P, Sahu AR. Efficacy of a standardized herbal preparation (Roidosanal®) in the treatment of hemorrhoids: A randomized, controlled, open-label multicentre study. J Ayurveda Integr Med 2014;5:117-24.

Source of Support: Financial support for patient-related procedures and examinations and study medications received from M/s Next Gen Pharma India Pvt. Ltd., New Delhi, **Conflict of Interest:** None declared.