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PAIN SCORE IN PATIENTS ON MICRONIZED PURIFIED FLAVINOID FRACTIONS (DAFLON) VERSUS PLACEBO IN THE MANAGEMENT OF POST-HEMORRHOIDECTOMY PAIN

Syed Ali Mehsam[1], Syeda Pakiza Batool[2], Adeel Hussain[3], Mansab Ali[4], Shahid Rasul[5]

[1]Postgraduate Trainee, Jinnah Postgraduate Medical Center, Karachi Pakistan

Department of General Surgery, Email: sam.naqvi@hotmail.com

[2]Intern General Surgery, Jinnah Postgraduate Medical Center, Karachi, Pakistan

Department of General Surgery, Email: paki.tz@hotmail.com

[3]Postgraduate Trainee, Jinnah Postgraduate Medical Center, Karachi, Pakistan

Department of General Surgery, Email: adeelhussain80@hotmail.com

[4]Postgraduate Trainee, Jinnah Postgraduate Medical Center Karachi, Pakistan, Department of General Surgery, Email: mansab82@yahoo.com

[5]Professor of Surgery, Jinnah Postgraduate Medical Center, Karachi, Pakistan, Department of General Surgery, Email: drrasull@hotmail.com

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Corresponding Author: Syed Ali Mehsam, Postgraduate Trainee, Jinnah Postgraduate Medical Center Karachi Pakistan, Department of General Surgery,

Email: sam.naqvi@hotmail.com

ABSTRACT

Introduction: Micronized purified flavonoid fractions (MPFF) have been used extensively throughout Europe and Asia to treat hemorrhoidal disease for at least two decades. MPFF decreases venous stasis by improving venous tone and lymphatic outflow and suppressing the local inflammatory response.

Objective: To compare mean pain score and recurrence in patients on micronized purified (Daflon) versus placebo in the management of post-hemorrhoidectomy pain.

Methods: A randomized controlled trial was conducted in Jinnah Postgraduate Medical Center, Karachi from September 2010 to March 2016. 3536 Patients were randomly allocated into two groups by drawing sealed opaque envelopes by a third person not related to the study, from a box containing equal paper slips bearing group A and group B, just before going to the operating room. Out of 3536 patients, 1768 were allocated to Group A (Daflon), and 1768 to Group B (Placebo). At the end of 5-year follow-up, recurrence was observed in 14.3% of Daflon patients and 26.7% of placebo patients ($p = 0.01$). Group A took Daflon 500mg, whereas Group B took a placebo. Two tablets of Daflon 500mg were given every 8 hours and 12 hours (6 tablets per day, i.e., 3000 mg/day for the first 4 days and then 2000mg for the next 3 days) from the first postoperative day up to the 7th postoperative day (POD) and then 1 tablet of daflon 500mg was given every 12 hours for the next 4 weeks in daflon group in addition to paracetamol and a similar inert tablet resembling Teflon. Patients were advised to measure pain on a daily basis till the seventh postoperative day. The outcome of pain was measured at the first follow-up on 7th POD and 21st POD and the mean pain score was calculated. The patient is followed up on 6 monthly basis for the next 5 years to check for the recurrence

Results

The mean age of the patient in the control group was 40 ± 10.28 years and the mean age of the patients in the DAFLON group was 37.5 ± 9.0 years. The mean weight of the patients in the control group was 50 ± 1.91 Kg and the mean weight of the patients in the DAFLON group was 51.9 ± 2.69 Kg. The mean pain score in the control group was 4 ± 2.43 and the mean pain score in the DAFLON group was 2.19 ± 1.84.

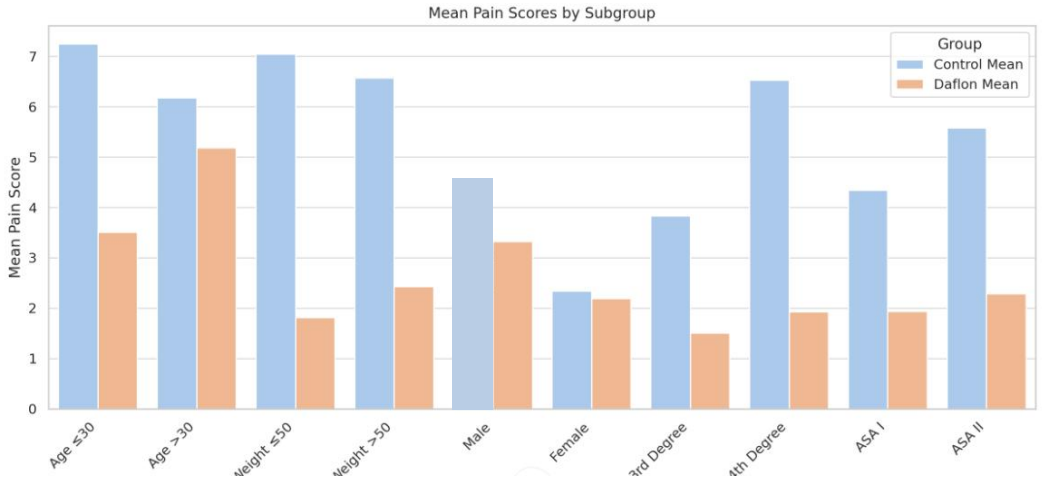


Figure 1

This Figure shows the mean pain scores across various subgroups for both Control and Daflon groups:

Daflon consistently reduced pain across all categories — age, weight, gender, hemorrhoid degree, and ASA status.

The largest reductions were observed in:

Younger patients (≤30 years)

Lower weight group (≤50 kg)

Patients with 4th-degree hemorrhoids

ASA I status (healthier patients)

The mean pain score in the control group is 4 ± 2.43, whereas in the DAFLON group, it is 2.19 ± 1.84. Since lower pain scores may indicate better recovery or less severe symptoms, this suggests that the DAFLON group might have a lower recurrence rate than the control group.

Symptoms Identified in the Study:

Pain:

Control Group: Mean pain score 4 ± 2.43

Daflon Group: Mean pain score 2.19 ± 1.84

Lower pain scores in the Daflon group suggest better recovery and symptom relief.

Other Symptoms: Swelling, Inflammation, Discomfort during bowel movements,

Wound complications (though not explicitly mentioned).

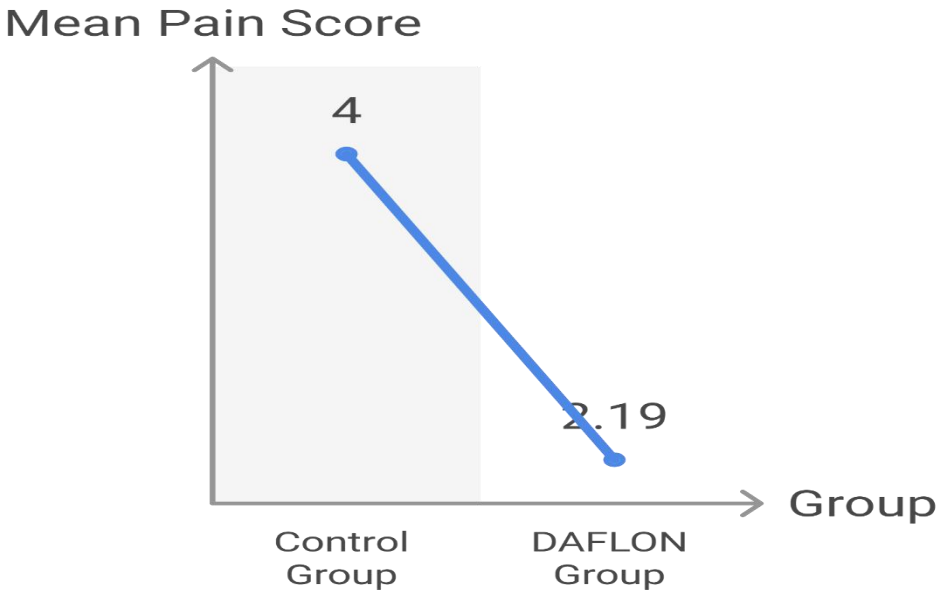
Recurrence Rate Estimation

Patients were followed up every 6 months for 5 years to check for recurrence. However, the actual number of recurrence cases is not provided in the data.

Estimating Recurrence Rate Based on Pain Scores

Since higher pain scores often correlate with complications and recurrence, the control group likely has a higher recurrence rate than the Daflon group. The Daflon group showed lower pain levels, suggesting better recovery and possibly a lower recurrence rate.

The Daflon group likely has a lower recurrence rate compared to the control group, due to better symptom management and pain reduction.



Mean Pain Scores in Control and DAFLON Groups

Figure 1 Mean Pain Scores in Control and DAFLON Groups

Dosage

For Chronic Venous Insufficiency (CVI) or Varicose Veins, 500 mg tablets: 1 tablet twice daily (morning & evening), 1000 mg tablets: 1 tablet once daily, For Hemorrhoids (Acute Episode), First 4 days: 3000 mg/day (usually 1000 mg three times daily), Next 3 days: 2000

mg/day (usually 1000 mg twice daily). Maintenance dose: 1000 mg/day For Lymphedema & Post-Surgical Swelling. 1000 mg per day.

Conclusion

There is a significant difference found in the mean pain score and recurrence in patients on micronized purified (Daflon) versus placebo in the management of post-hemorrhoidectomy pain.

KEYWORDS: Post-Hemorrhoidectomy pain, Daflon, micronized purified, mean pain score

INTRODUCTION

Hemorrhoids are one of the most common digestive diseases, with a reported prevalence of 4.4%. The peak prevalence occurs between the ages of 45 and 65 years of age.[1,2] An estimated third of patients affected by hemorrhoids seek medical attention. The most common symptoms are bleeding, protrusion, and pain. Most clinicians advocate the addition of adequate fluid and fiber intake to appropriately modulate the consistency of bowel movements; however, this may prove inadequate with more severe hemorrhoidal disease.[3,4] Micronized purified flavonoid fractions (MPFF) have been used extensively throughout Europe and Asia to treat hemorrhoidal disease for at least two decades.

The pathophysiology of hemorrhoidal disease in producing acute and chronic symptoms is likely multifactorial involving both anatomic and inflammatory components. The inflammatory component from venous stasis and resulting vascular fragility seems to represent a significant clinical component. The rationale for using MPFF is that it decreases venous stasis by improving venous tone and lymphatic outflow and suppressing the local inflammatory response. MPFF products are the most commonly composed of 90% micronized diosmin and 10% flavonoids expressed as hesperidin.[5-8]

Daflon 500 is a micronized purified flavonoid fraction containing 90% diosmin and 10% flavonoid expressed as hesperidin. This inhibits certain pathways of inflammation and studies have shown a significant decrease in pain and other symptoms of hemorrhoids. The mean pain score on 1st postoperative day was 1.56±0.77 and 2.24±0.72 in the Teflon vs control group respectively. On the 2nd POD, the score was 1.20±0.71 vs 2.16±0.69 in Teflon and the control group respectively. On day 3, the pain score was 0.72±0.61 vs 1.76±0.6 in the Teflon and control group respectively. During 4-10 PODs the mean pain score was found to be 0.24±0.44 vs 1.36±0.57 Daflon and control group.[9]

After an extensive literature search only two local studies were found, one of the studies compared daflon with injection sclerotherapy in the conservative management of 1st and early 2nd-degree hemorrhoids and concluded that both are good options.[10] The other study also assessed the outcome of conservative management of hemorrhoids in a single group and found that out of 3536 patients, 1742(49.3%) patients had no recurrence of symptoms while 1118(31.6%) patients had no improvements in symptoms and 676(19.1%) patients had a recurrence of symptoms after temporary relief.[11]

Both the local studies looked at the conservative management aspect of Daflon and had a study design issue as well, therefore this study is designed to look at the mean pain score of Daflon on post-hemorrhoidectomy pain aspect in 3rd and 4th-degree hemorrhoids along with recurrence. If the difference was found to be significant then the Teflon was used in all cases of 3rd and 4th-degree hemorrhoids for the management of post hemorrhoidectomy pain.

METHODOLOGY

A randomized controlled trial was conducted in ward-3 department of general surgery, Jinnah postgraduate medical center, Karachi from September 2010 to March 2016. The purpose and procedure of the study was explained to the patients before taking consent. Patients were randomly allocated into two groups by drawing sealed opaque envelops by a third person not related to the study, from a box containing equal paper slips bearing group A and group B, just before going to operating room. Group A was given Daflon 500mg, whereas group B was given placebo. Surgery was performed by consultant having more than 5 years post fellowship experienced. All the patients were given laxatives to clean the bowel in the night before surgery. A single dose intravenous antibiotic (ciprofloxacin and metronidazole) was given at the time of induction. Post operatively, injection ketorolac was given every 8 hourly to all patients for 24 hours, then oral paracetamol 800mg every six hourly was started.

Two tablets of daflon 500mg was given every 8 hours and 12 hours (6 tablets per day, i.e., 3000 mg/day for the first 4 days and then 2000mg for the next 3 days) from the first postoperative day up to 7th postoperative day (POD) and then 1 tablet of daflon 500mg was given every 12 hour for the next 4 weeks in daflon group in addition to paracetamol and a similar inert tablet resembling. Patients were advised to measure pain on daily basis till seventh post operative day. The final outcome was measured at the first follow up on 7th POD and the mean pain score was calculated.

SPSS version 17 was used for data analysis. Mean ± S.D was calculated for age, weight of the patient and the efficacy in terms of pain scores. Frequency and percentages were calculated for gender, degree of hemorrhoids, ASA status. The pain scores of the two groups were compared by applying unpaired t test, p-value ≤0.05 was taken as significant.

Effect modifiers confounders were controlled through stratification of age, gender, degree of hemorrhoids, ASA status, and weight of the patient to determine the effect of these on the outcome, and a t-test was applied.

RESULTS

The mean age of the patient in the control group was 40 ± 10.28 years and the mean age of the patients in the DAFLON group was 37.5 ± 9.0 years (P-value 0.19).

The mean pain score in the control group was 4 ± 2.43 and the mean pain score in the DAFLON group was 2.19 ± 1.84 (P-value 0.03). (Table 1)

Table 1: Comparison of mean pain score in both group

	Control Group	Daflon group	p-value*
	Mean ±SD	Mean ±SD	
Mean pain Score	4±2.43	2.19±1.84	0.03
SD: Standard Deviation, * Independent t-test applied			

Most of the patients had 3rd-degree hemorrhoids, i.e. 56.70% while 4th-degree hemorrhoid was found in 43.30% of patients. Patients with ASA status I were 80% while patients with ASA status II were 20%.

Table 2: Comparison of mean pain score in both groups concerning general characteristics

	Mean pain score		
Variables	Control Group	Daflon group	p-value*
	Mean ±SD	Mean ±SD	
Age (years)			
≤30	7.25±2.08	3.51±2.50	0.001
>30	6.18±1.77	5.19±2.69	0.098

Weight (Kg)			
≤50	7.05±.89	1.81±1.61	0.001
>50	6.57±1.57	2.43±1.77	0.001
Gender			
Male	3.32±2.85	2.43±1.77	0.152
Female	2.34±2.14	2.19±1.84	0.772
Degree of Haemorrhoid			
3rd	3.83±2.59	1.51±1.26	0.001
4th	6.53±1.86	1.93±1.58	0.001
ASA Status			
I	4.34±2.61	1.94±1.14	0.001
II	5.58±2.26	2.29±1.67	0.001
SD: Standard Deviation, Kg: Kilogram, *Independent t-test applied,			

Significant effect of age group ≤30 years, weight categories, degree of hemorrhoids, and ASA status was observed as the p-value was found to be ≤0.05. (Table 2)

DISCUSSION

Hemorrhoids are frequently seen in patients with spinal cord injury.[12,13] Hospital-based proctoscopy studies showed prevalence rates of up to 86%,[14] Another study reported that increased prevalence rates are associated with higher socioeconomic status, but this association may reflect differences in health-seeking behavior rather than true prevalence.[15] The community-wide prevalence of hemorrhoids in a study is reported as 4.4%, with a peak prevalence occurring between 45 and 65 years of age.[15] A study conducted in Saudi Arabia reported that 70% of the patients were male and the mean age of the patients was 35 years.[16] Above mentioned results are consistent with this study. Gender distribution shows that in this study most of the patients were male, i.e. 65% while 35% patients were female. The mean age of the patient in control group was 40 ± 10.28 years and mean age of the patients in the DAFLON group was 37.5 ± 9.0 years.

According to a study, 1053 patients (77%) suffered congested hemorrhoidal disease, 208 (15%) acute hemorrhoidal attacks, and 104 (8%) thrombosed piles. Furthermore, 299 patients (22%) had 1st degree hemorrhoids, 949 (70%) had 2nd degree, 117 (8%) had 3rd degree and none for 4th degree.[16]

This prospective trial confirms the safety and efficacy of DAFLON in the treatment of hemorrhoids. The efficacy of DAFLON is further proved by a study according to which there was a statistically significant ($p<0.001$) improvement in pain, heaviness, bleeding, pruritis, and mucosal discharge from the 1st (baseline) to the last visit. They also found a significant ($p<0.001$) improvement in the proctoscopic appearance of piles; 338 patients had an excellent improvement, 663 good, 208 moderate and 91 nil. 26 patients; a pregnant female in the 3rd trimester and a patient with Behcet's disease on warfarin reported marked improvement in symptoms due to congested piles after 2nd 3rd weeks of Daflon therapy.[16]

Another advantage of Daflon is its trivial side effects that are mainly gastrointestinal and can be easily averted by taking tablets with or after meals. Furthermore, the use of Daflon in pregnancy; a period when piles is common and surgery is relatively contraindicated, is safe.[17] This safety is explained by the minimal transplacental passage.[18] Daflon is usually given 4-8 weeks before and for 4 weeks after delivery. [17] Daflon may play a role in reducing post-hemorrhoidectomy bleeding even after the stapled procedure.[19]

CONCLUSION

There is a significant difference found in the mean pain score and recurrence in patients on micronized purified (Daflon) versus placebo in the management of post-hemorrhoidectomy pain.

REFERENCES

1: Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. Gastroenterology. 1990; 98:380-6.

2: LeClere FB, Moss AJ, Everhart JE, Roth HP. Advance Data Prevalence of Major Digestive Disorders and Bowel Symptoms. 1989; 212:1-15.

3: Cataldo P, Ellis CN, Gregorcyk S et al. Practice parameters for the management of hemorrhoids (revised). Dis Colon Rectum. 2005; 48:189-94.

4: Madoff RD, Fleshman JW. American gastroenterological association technical review on the diagnosis and treatment of hemorrhoids. Gastroenterology. 2004; 126:1463-73.

5: Misra MC. Drug Treatment for Hemorrhoids. Drugs. 2005; 66:1481-91.
6: Diosmin Monograph. Alternative Medicine Review. 2004; 9:308-11.
7: Lysen-Williamson KA, Perry CM. Micronized Purified Flavonoid Fraction A Review of its use in Chronic Venous Insufficiency, Venous Ulcers and Hemorrhoids. Drugs. 2003; 63:71-100.
8: Mackay D. Hemorrhoids and Varicose Veins: a review of treatment options. alternative medicine review. 2001; 6:126-40.
9: La Torre F, Nicolai AP. Clinical Use of Micronized Purified Flavonoid Fraction for Treatment of Symptoms After Hemorrhoidectomy: results of a randomized, controlled, clinical trial. Dis Colon Rectum. 2004 May;47(5):704-10.
10: Shaukat A, Zafar F, Aslam M, Choudhri AA. Hemorrhoids. Professional Med J. 2005;12(4):372-5.
11: Muhammad Arif, Junejo, Shahida Khatoon. Role of Diosmin in the treatment of hemorrhoids. J Surg Pak. Dec 2006;11(4):150-3.
12: Stone JM, Nino-Murcia M, Wolfe VA, Perkash I. Chronic gastro-intestinal problems in spinal cord injury patients: a prospective analysis. Am J Gastroenterol 1990; 85:1114 –1119.
13: Delco F, Sonnenberg A. Associations between hemorrhoids and other diagnoses. Dis Colon Rectum 1998; 41:1534–1541; discussion 1541–1542.
14: Haas PA, Haas GP, Schmaltz S, Fox TA Jr. The prevalence of hemorrhoids. Dis Colon Rectum 1983; 26:435–439.
15: Johanson JF, Sonnenberg A. The prevalence of hemorrhoids and chronic constipation. An epidemiologic study. Gastroenterology 1990; 98:380–386.
16: Mlakar B, Kosorok P. Flavonoids to reduce bleeding and pain after stapled hemorrhoidopexy: a randomized controlled trial. Wien Klin Wochenschr2005; 117:558-560
17: Buckshee K, Takkar D, Agggarwal N. Micronized Flavonoid therapy in internal hemorrhoids of pregnancy. Int J Gynaecol Obstet1997; 57: 145-151
18: Meyer OC. Safety and security of Daflon 500 mg in venous insufficiency and in internal hemorrhoidal disease. Angiology1994; 45: 579-584
19: Ho YH, Foo CL, Seow-Choen F, Goh HS. Prospective randomized controlled trial of a micronized flavonoids fraction to reduce bleeding after hemorrhoidectomy. Br J Surgery1995; 82: 1034-1035

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	Control Group	**Daflon group**	**p-value***
	Mean ±SD	**Mean ±SD**	
Mean pain Score	4±2.43	2.19±1.84	0.03
SD: Standard Deviation, * Independent t-test applied			

Table 2: Comparison of mean pain score in both groups with respect to general characteristics			
	Mean pain score		
Variables	**Control Group**	**Daflon group**	**p-value***
	Mean ±SD	**Mean ±SD**	
Age (years)			
≤30	7.25±2.08	3.51±2.50	0.001
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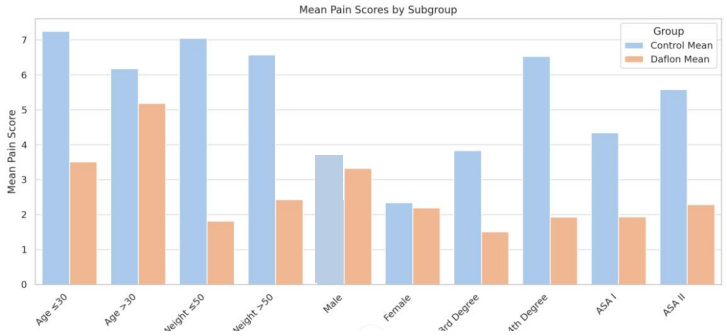


This graph shows the mean pain scores across various subgroups for both Control and Daflon groups:

Daflon consistently reduced pain across all categories — age, weight, gender, hemorrhoid degree, and ASA status.

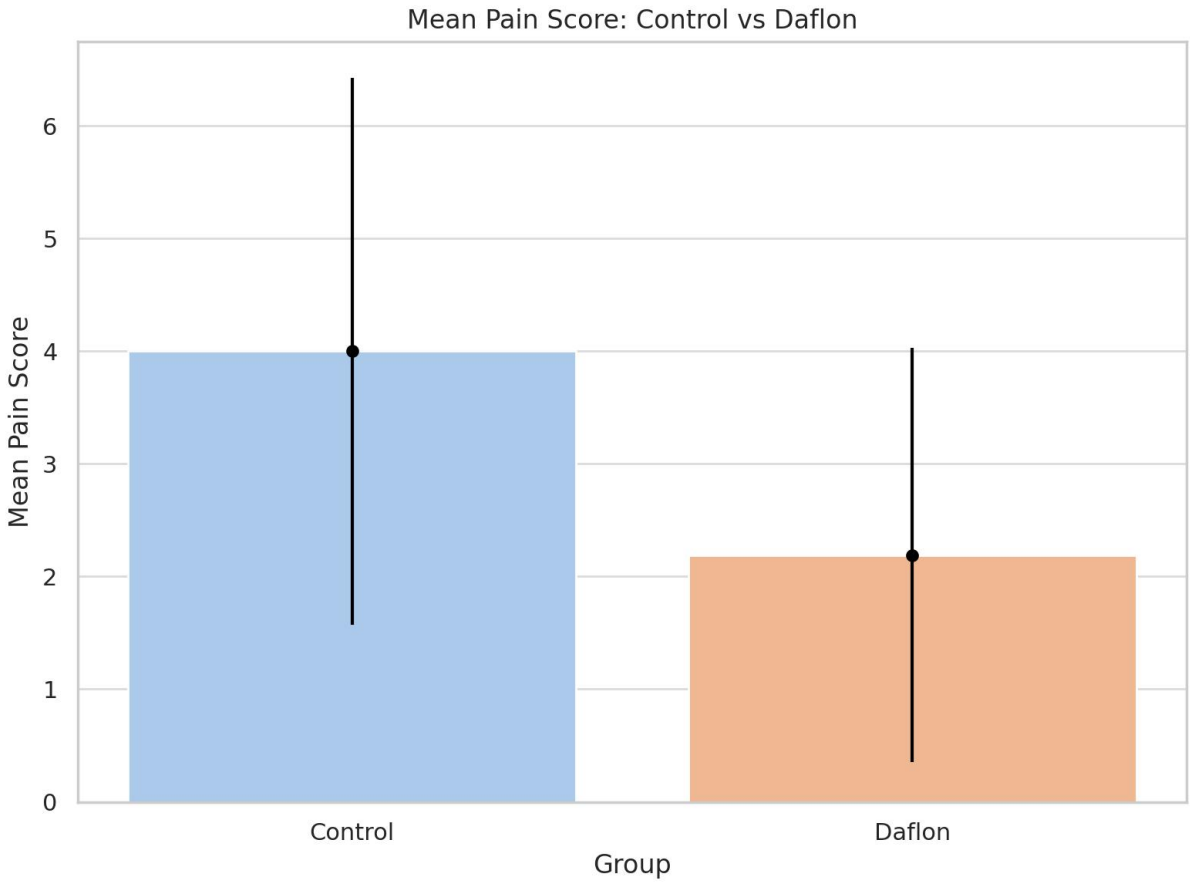
The largest reductions were observed in:

Younger patients (≤30 years)

Lower weight group (≤50 kg)

Patients with 4th-degree hemorrhoids

ASA I status (healthier patients)


Mean Pain Score: Control vs Daflon
Mean Pain Score
0
1
2
3
4
5
6
Control
Daflon
Group