RESEARCH PAPER

A Randomised Control Study Using Oralmicronized Purified Flavonoid Fraction Versustopical Glycerine Magnesium Sulphate Application In The Surgical Management Of Grade 3 And 4 External Hemorrhoids

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ABSTRACT

Background

Hemorrhoidal disease is a common anorectal condition that significantly affects patient quality of life. Advanced hemorrhoids, particularly Grade III and IV external hemorrhoids, often require surgical management due to persistent prolapse, bleeding, and pain. Postoperative complications such as edema, inflammation, and delayed wound healing remain significant concerns. Pharmacological adjuncts aimed at reducing inflammation and improving microcirculation may enhance postoperative outcomes. Oral micronized purified flavonoid fraction (MPFF) has demonstrated venotonic, anti-inflammatory, and capillary-protective effects, whereas topical glycerine magnesium sulphate (GMS) primarily acts locally through osmotic mechanisms to reduce edema.

Aim:To evaluate and compare the effectiveness of oral micronized purified flavonoid fraction and topical glycerine magnesium sulphate in the surgical management of Grade III and IV external hemorrhoids.

Objectives

- To assess the effectiveness of oral MPFF and topical GMS in hemorrhoid management.
- To analyze intraoperative bleeding in patients receiving MPFF versus GMS.
- To evaluate postoperative bleeding episodes in both treatment groups.
- To compare postoperative pain using the Visual Analog Scale (VAS).
- To examine differences in outcomes based on age and gender.
- To determine the relative effectiveness of both therapeutic approaches.

Methodology

This study was conducted as a randomized controlled trial in the Department of General Surgery at SRM Medical College Hospital and Research Centre, Tamil Nadu. A total of 100 patients diagnosed with Grade III or IV external hemorrhoids were included and randomly allocated into two groups of 50 participants each.

Group A received oral micronized purified flavonoid fraction (Daflon 500 mg, two tablets twice daily) for four weeks preoperatively, followed by hemorrhoidectomy.

Group B received topical glycerine magnesium sulphate application for the same duration before undergoing hemorrhoidectomy.

Primary outcomes measured included reduction in hemorrhoid size, intraoperative bleeding, postoperative bleeding, and postoperative pain scores measured using the Visual Analog Scale. Secondary outcomes included postoperative complications, recovery time, and demographic influences such as age and gender.

Statistical analysis was performed using SPSS version 26. Continuous variables were analyzed using independent t-tests or Mann-Whitney U tests, while categorical variables were analyzed using chi-square tests. A p-value <0.05 was considered statistically significant.

Results

It is expected that oral MPFF will demonstrate superior systemic effects through improved venous tone, reduced capillary permeability, and anti-inflammatory action, potentially resulting in reduced intraoperative bleeding and improved wound healing. Topical GMS is expected to provide rapid localized relief by reducing postoperative edema and associated pain.

Conclusion

Both MPFF and topical GMS play beneficial roles in the perioperative management of advanced hemorrhoids through different mechanisms. MPFF provides systemic vascular and anti-inflammatory benefits, while GMS offers local edema control and symptomatic relief. Comparative evaluation of these interventions may help optimize postoperative recovery strategies in hemorrhoidectomy patients and guide future clinical practice.

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Keywords: Hemorrhoids; Hemorrhoidectomy; Micronized purified flavonoid fraction; Glycerine magnesium sulphate; Randomized controlled trial; Postoperative pain

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Introduction

Hemorrhoidal disease is one of the most common anorectal conditions worldwide and significantly affects patient quality of life. It is characterized by pathological enlargement and symptomatic prolapse of the anal vascular cushions. While early-stage hemorrhoids can often be managed conservatively, advanced disease—particularly Grade III and IV hemorrhoids—frequently requires surgical intervention. Grade III hemorrhoids prolapse during defecation and require manual reduction, whereas Grade IV hemorrhoids remain permanently prolapsed and irreducible. These advanced stages are frequently associated with complications such as thrombosis, persistent bleeding, mucosal ulceration, and severe pain, making surgical management the preferred treatment modality. Excisional hemorrhoidectomy remains the gold standard for the treatment of advanced hemorrhoids due to its low recurrence rate and definitive removal of diseased tissue. However, postoperative morbidity remains significant, with complications including severe pain, edema, bleeding, delayed wound healing, and prolonged hospital stay. Therefore, optimizing perioperative management strategies is essential to improve patient outcomes and reduce postoperative morbidity.One promising approach involves the use of pharmacological agents that target the vascular and inflammatory components of hemorrhoidal disease. Oral micronized purified flavonoid fraction (MPFF), composed primarily of diosmin and hesperidin, has demonstrated venotonic, anti-inflammatory, and capillary-protective effects. These properties enhance venous tone, reduce capillary permeability, and improve lymphatic drainage, potentially reducing postoperative complications.Topical glycerine magnesium sulphate (GMS) represents another therapeutic option that acts locally through osmotic mechanisms to reduce edema and tissue tension at the surgical site. While GMS provides symptomatic relief through local edema reduction, it lacks systemic anti-inflammatory and venotonic effects.Although both MPFF and GMS have been individually studied in hemorrhoidal disease, direct comparisons between these two interventions in the perioperative management of advanced hemorrhoids are limited. This randomized controlled study therefore aimed to compare the effectiveness of oral MPFF and topical GMS as adjuncts in the surgical management of Grade III and IV external hemorrhoids.

Materials and Methods

Study Design

This study was designed as a **prospective randomized controlled trial** conducted at the Department of General Surgery, SRM Medical College Hospital and Research Centre, Tamil Nadu.

Study Population

Patients presenting with Grade III or Grade IV external hemorrhoids requiring surgical management were considered for inclusion.

Inclusion criteria

- Patients aged ≥18 years
- Diagnosed with Grade III or Grade IV external hemorrhoids
- Planned for elective hemorrhoidectomy

Exclusion criteria

- Patients with inflammatory bowel disease
- Coagulopathy or anticoagulant therapy
- Previous anorectal surgery
- Pregnancy
- Known allergy to study medications

Sample Size

The sample size was determined based on prior research comparing MPFF with topical therapies for haemorrhoids. With an expected effect size of .5, a power of 80%, and a significance threshold of 5%, the minimum necessary sample size was 60 (30 each group). The sample size was augmented to 100 (50 each group) to accommodate probable dropouts and improve statistical robustness. This adjustment ensured reliable detection of clinically significant differences in primary outcomes, such as bleeding and pain reduction.

$$n \geq \frac{(Z_{1-\alpha/2} \times Z_{1-\beta})^2 (P_1 - P_2)^2}{(P_2 - P_1)^2}$$

Total sample size =60
Adjusted to 100 (n1-50 ; n2- 50)

Randomization

Patients were randomly assigned into two treatment groups using a computer-generated randomization sequence.

Group A (Oral MPFF group)

Patients received **micronized purified flavonoid fraction (Daflon 500 mg)** two tablets twice daily for four weeks prior to surgery.

Group B (Topical GMS group)

Patients received **topical glycerine magnesium sulphate application** to the hemorrhoidal area for four weeks prior to surgery.

All patients subsequently underwent standard excisional hemorrhoidectomy.

Outcome Measures

Primary outcomes

- Intraoperative bleeding severity
- Postoperative bleeding
- Postoperative pain assessed using Visual Analog Scale (VAS)

Secondary outcomes

- Duration of surgery
- Postoperative complications
- Hospital stay
- Surgeon satisfaction score
- Patient satisfaction score

Data Collection

Data were collected using structured case record forms including demographic characteristics, operative findings, and postoperative outcomes.

Statistical Analysis

Data were analyzed using **SPSS version 26**. Continuous variables were expressed as mean ± standard deviation and compared using independent t-tests. Categorical variables were analyzed using the chi-square test. Statistical significance was defined as $p < 0.05$.

Results

Study Population

A total of **100 patients** diagnosed with Grade III or Grade IV external hemorrhoids were included in this randomized controlled study. Participants were equally divided into two groups:

- **Group A:** Oral micronized purified flavonoid fraction (MPFF) (n = 50)
- **Group B:** Topical glycerine magnesium sulphate (GMS) (n = 50)

Both groups underwent hemorrhoidectomy after four weeks of preoperative therapy.

Baseline Characteristics

Gender Distribution

The overall study population consisted of **58 males (58%) and 42 females (42%)**.

Gender	Oral MPFF (n=50)	Topical GMS (n=50)	Total
Male	31 (62%)	27 (54%)	58
Female	19 (38%)	23 (46%)	42

The distribution of gender was comparable between the two groups, indicating adequate randomization and minimizing potential gender-related bias in treatment outcomes.

Distribution of Hemorrhoid Grade

The severity of hemorrhoidal disease at baseline was similar in both treatment groups.

Table 1. Distribution of Hemorrhoid Grade

Grade	Oral MPFF (n=50)	Topical GMS (n=50)	Total (n=100)	χ^2	p-value
Grade III	34	28	62		
Grade IV	16	22	38	1.52	0.22
Total	50	50	100		

There was **no statistically significant difference** in the distribution of hemorrhoid grades between the two groups, confirming comparability of disease severity at baseline.

Intraoperative Outcomes

Intraoperative Bleeding

The severity of intraoperative bleeding differed significantly between the two treatment groups.

Table 2. Intraoperative Bleeding Severity

Bleeding Severity	Oral MPFF (n=50)	Topical GMS (n=50)	Total	χ^2	p-value
Mild	41 (82%)	22 (44%)	63		
Moderate	9 (18%)	28 (56%)	37	15.486	<0.001

Bleeding Severity	Oral MPFF (n=50)	Topical GMS (n=50)	Total	χ^2	p-value
Severe	0	0	0		
Total	50	50	100		

Mild bleeding was significantly more common in the **oral MPFF group**, whereas moderate bleeding was more frequent in the **topical GMS group**, indicating superior intraoperative hemostasis with systemic flavonoid therapy.

Duration of Surgery

The mean duration of surgery was shorter in the oral MPFF group.

Table 3. Comparison of Duration of Surgery

Group	Mean Duration (minutes) ± SD	t value	p-value
Oral MPFF	50.30 ± 10.22		
Topical GMS	53.68 ± 6.44	−1.98	0.041

This difference was statistically significant, suggesting improved operative conditions in patients treated with oral MPFF.

Surgeon Satisfaction

Surgeon satisfaction was evaluated across different operative steps during hemorrhoidectomy.

Table 4. Surgeon Satisfaction Scores

Surgical Step	Oral MPFF (Mean ± SD)	Topical GMS (Mean ± SD)	t value	p-value
Hemorrhoidal dissection	4.5 ± 0.6	3.8 ± 0.7	4.12	0.001
Pedicle ligation	4.6 ± 0.5	3.9 ± 0.6	4.35	<0.001
Transfixation	4.4 ± 0.6	3.7 ± 0.7	3.98	0.002
Excision of hemorrhoidal tissue	4.5 ± 0.5	3.8 ± 0.6	4.26	<0.001
Post-excision hemostasis	4.7 ± 0.4	3.6 ± 0.7	5.10	<0.001

Across all surgical steps, the oral MPFF group demonstrated significantly higher satisfaction scores, reflecting improved operative ease and better intraoperative conditions.

Postoperative Outcomes

Postoperative Complications

The incidence of postoperative complications differed significantly between the two groups.

Table 5. Distribution of Postoperative Complications

Complication	Oral MPFF (n=50)	Topical GMS (n=50)
Hemorrhage	1	8
Infection	2	4
Anal incontinence	1	5
Anal stricture	3	11
No complications	43	22

Statistical analysis demonstrated a **significant reduction in complications in the oral MPFF group** ($\chi^2 = 20.133$, $p = 0.004$).

Postoperative Pain

Pain severity was evaluated using the **Visual Analog Scale (VAS)**.

Table 6. Postoperative Pain Severity

Pain Severity (VAS)	Oral MPFF (n=50)	Topical GMS (n=50)	χ^2	p-value
Mild (0–3)	33	18		
Moderate (4–6)	16	25	10.887	0.004
Severe (7–10)	1	7		

Patients receiving oral MPFF experienced significantly less postoperative pain compared with those receiving topical therapy.

Postoperative Hospital Stay
Hospital stay was significantly shorter in the oral MPFF group.

Table 7. Comparison of Postoperative Hospital Stay

Hospital Stay	Oral MPFF (Mean ± SD)	Topical GMS (Mean ± SD)	t value	p-value
≤ 1 week	5.92 ± 0.80	7.00 ± 0.00	−6.90	<0.001
1–2 weeks	8.92 ± 0.88	10.64 ± 1.93	−5.09	<0.001

These findings indicate faster postoperative recovery among patients receiving oral MPFF.

Patient Satisfaction
Patient satisfaction differed significantly between the two treatment groups.

Table 8. Patient Satisfaction Scores

Satisfaction Level	Oral MPFF (n=50)	Topical GMS (n=50)
Extremely satisfied	25	5
Satisfied	23	21
Not satisfied	2	24

The difference in satisfaction was **highly statistically significant** ($\chi^2 = 32.04$, $p < 0.001$).

Discussion
This randomized controlled study compared the perioperative effectiveness of oral micronized purified flavonoid fraction and topical glycerine magnesium sulphate in patients undergoing hemorrhoidectomy for Grade III and IV external hemorrhoids. The results demonstrate clear superiority of systemic flavonoid therapy across multiple intraoperative and postoperative outcomes.Intraoperative bleeding was significantly reduced in the MPFF group, which may be attributed to improved venous tone and reduced capillary permeability induced by flavonoid therapy. Similar findings have been reported in previous studies demonstrating enhanced hemostasis and improved surgical field visibility with MPFF therapy.
Postoperative complications were also significantly lower in patients receiving MPFF. The reduced incidence of hemorrhage, anal stricture, and incontinence suggests improved wound healing and reduced inflammatory response. These findings are consistent with previous randomized trials that have demonstrated anti-inflammatory and microcirculatory benefits of flavonoid therapy.Pain control is a critical determinant of recovery after hemorrhoidectomy. In this study, the oral MPFF group experienced significantly lower postoperative pain scores compared with the topical therapy group. The systemic anti-inflammatory effects of MPFF likely contributed to this outcome.Hospital stay was significantly shorter in the oral therapy group, reflecting improved recovery and reduced postoperative morbidity. Shorter hospitalization has important implications for healthcare resource utilization and patient quality of life.Patient satisfaction outcomes strongly favored oral MPFF therapy. Higher satisfaction scores likely reflect the combined benefits of reduced pain, fewer complications, and faster recovery.Although topical glycerine magnesium sulphate may provide local edema control, it lacks systemic venotonic and anti-inflammatory properties, which likely explains its inferior performance compared with oral MPFF in this study.

Limitations
The research was conducted at a **single center with a relatively limited sample size**, which may affect the **generalizability of the findings** to broader populations. There was also a **difference in age distribution between the study groups**, which could introduce some degree of demographic imbalance, although the **severity of hemorrhoidal disease was comparable** between groups.The study primarily evaluated **early postoperative outcomes**, and **long-term follow-up was not performed**, limiting the ability to assess **recurrence rates, sustained symptom relief, and long-term functional outcomes** such as continence and quality of life. Additionally, **surgeon satisfaction**, included as an outcome parameter, is inherently **subjective** and may vary depending on individual experience and expectations.

Conclusion
This randomized controlled trial demonstrates that **oral micronized purified flavonoid fraction is superior to**

topical glycerine magnesium sulphate as a perioperative adjunct in hemorrhoidectomy for Grade III and IV external hemorrhoids.

MPFF significantly improves intraoperative hemostasis, reduces postoperative pain and complications, shortens hospital stay, and enhances patient satisfaction.

These findings support the incorporation of **systemic flavonoid therapy into perioperative management protocols for advanced hemorrhoidal disease**.

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