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Association of Topical Glyceryl Trinitrate (0.2%) Use With Resting Anal Canal Pressure and Symptom Severity in Patients With Symptomatic Haemorrhoids: A Cross-Sectional Observational Study

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Abstract

Objective:
Elevated resting anal canal pressure has been implicated in the pathophysiology of symptomatic haemorrhoids, contributing to pain, discomfort, and impaired venous drainage. Topical glyceryl trinitrate (GTN) 0.2% ointment induces smooth muscle relaxation via nitric oxide–mediated pathways and is known to reduce anal sphincter tone. While widely used in anal fissure management, evidence regarding its association with symptom relief in haemorrhoid patients with high resting anal pressure remains limited in real-world clinical settings.

Material and Methods:
This cross-sectional observational study was conducted in outpatient clinics in Karachi, Pakistan. Adults aged 18–65 years with clinically diagnosed internal haemorrhoids were enrolled. Participants were categorized into GTN-exposed (≥7 days of topical GTN 0.2% use) and non-exposed groups. Resting anal canal pressure was measured using anorectal manometry. Symptom severity was assessed using a structured composite score evaluating pain, bleeding, pruritus, and defecatory discomfort. Between-group comparisons and multivariable analyses were performed to assess associations between GTN use, anal pressure, and symptom burden.

Results:
Patients using topical GTN demonstrated lower resting anal canal pressures and reduced symptom severity compared with non-exposed patients. Lower anal pressures were significantly associated with reduced pain and overall symptom scores. These associations remained significant after adjustment for age, haemorrhoid grade, constipation severity, and stool consistency.

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Conclusion:
Use of topical glyceryl trinitrate 0.2% ointment was associated with lower resting anal canal pressure and improved haemorrhoidal symptoms in this observational cohort. GTN may represent a useful adjunctive pharmacological option for symptom relief in haemorrhoid patients with elevated anal sphincter tone, warranting further controlled studies.

Keywords: *Pharmaceutical Preparations, glycerol trinitrate reductase, Hemorrhoids, Anal fissure, Drugs, Pharmacology*.

Introduction

Haemorrhoidal disease is one of the most common anorectal disorders seen in clinical practice[1]. The prevalence has been estimated from approximately 50% to 66% in the general population, and symptomatic haemorrhoids affecting up to one-third of adults at some point in their lives[2]. Patients with symptomatic haemorrhoids frequently present with rectal bleeding, anal pain, pruritus, irritation, and discomfort during defecation, leading to significant impairment in quality of life and increased healthcare utilization[3]. Although conservative measures such as dietary modification, stool softeners, and topical agents are first-line interventions, symptoms often persist despite these approaches, particularly when underlying anorectal physiological abnormalities are present[4]. One recognised contributor to symptom burden in haemorrhoidal disease is elevated resting anal canal pressure, which may exacerbate venous engorgement, increase straining discomfort, and alter anodermal perfusion[5]. In analogous anorectal conditions such as chronic anal fissure, topical glyceryl trinitrate (GTN) ointment has been shown to produce a significant reduction in resting anal sphincter tone via nitric oxide–mediated smooth muscle relaxation, effectively functioning as a “chemical sphincterotomy” and promoting symptomatic improvement[6]. In a prospective open-label study of patients with haemorrhoidal symptoms and high resting anal canal pressures, application of Rectogesic (glyceryl trinitrate 0.2%) three times daily for 14 days was associated with a statistically significant reduction in maximum resting anal canal pressure (mean 115.0 ± 40.4 mmHg vs. 94.7 ± 34.1 mmHg, $P < 0.001$) [7]. Significant improvements in rectal bleeding, pain, pruritus, irritation, and difficulty in bowel movement have also been seen[7]. These findings support the mechanistic plausibility that GTN’s smooth muscle–relaxing properties can alleviate anorectal hypertonia and thus relieve symptoms associated with haemorrhoidal disease[7].Despite this evidence, the use of topical GTN in haemorrhoids remains less well characterised than in anal fissure, and controlled observational data on its associations with both biomechanical outcomes (anal canal pressure) and patient-reported symptom severity are limited[8]. Post-haemorrhoidectomy studies and meta-analyses suggest that GTN ointment may reduce post-operative pain and opioid requirement, further indicating its potential analgesic and sphincter-relaxing effects in haemorrhoid-related discomfort. Nonetheless, existing literature

largely comprises interventional trials or analyses outside of common haemorrhoidal populations, highlighting a gap in real-world observational evidence[9]. Accordingly, we conducted a cross-sectional observational study to examine whether topical glyceryl trinitrate 0.2% use is associated with differences in resting anal canal pressure and symptom severity among patients with symptomatic haemorrhoids. By comparing anal pressure measurements and structured symptom scores between GTN-exposed and non-exposed participants in a clinical outpatient setting, this study aims to provide clinically relevant data on GTN's utility as an adjunctive therapeutic option in haemorrhoidal disease management.

Methods

This cross-sectional observational study was conducted to evaluate the association between topical glyceryl trinitrate (GTN) 0.2% ointment use with resting anal canal pressure and symptom severity among patients with symptomatic haemorrhoids. The study was carried out in outpatient general surgery and colorectal clinics in Karachi, Pakistan, where facilities for anorectal manometry were available. Data collection was performed over a defined study period following approval from the institutional ethics review committee.The targeted population comprised adult patients aged 18–65 years presenting with symptomatic internal haemorrhoids (Goligher grade I–III), diagnosed clinically by a consultant surgeon or colorectal specialist. Symptoms included rectal bleeding, anal pain, pruritus, irritation, and discomfort during defecation. Participants were categorized into two groups based on exposure status: those using topical glyceryl trinitrate 0.2% ointment for at least seven consecutive days as part of routine clinical management (GTN-exposed group), and those not using GTN and receiving standard conservative therapy alone (non-exposed group), as documented in medical records and patient interviews. Patients were excluded if anal fissure was the primary diagnosis, if they had undergone anorectal surgery within the preceding three months, or if they had inflammatory bowel disease, suspected anorectal malignancy, pregnancy or lactation, severe anaemia, hypotension, or known hypersensitivity to nitrates. Additional exclusion criteria included current use of phosphodiesterase-5 inhibitors, significant cardiovascular disease where nitrates are contraindicated, neurological disorders affecting anorectal function, or inability to tolerate anorectal manometry. Patients unable to provide informed consent were also excluded. A non-probability consecutive sampling technique was employed, whereby all eligible patients attending participating clinics during the study period were invited to participate until the required sample size was achieved. Sample size was calculated using G*Power software, assuming a moderate effect size (Cohen's d = 0.5) for differences in resting anal canal pressure between exposed and non-exposed groups, a power of 80%, and a two-tailed alpha of 0.05. This yielded a minimum requirement of 64 participants per group. To account for incomplete data and potential exclusions, a total sample of approximately 140–150 participants was targeted. Data were collected during a single study visit. After obtaining written informed consent, demographic and clinical information were recorded, including age, sex, body mass index, haemorrhoid grade, duration of symptoms, bowel habits, constipation history, stool form (Bristol Stool Scale), fibre intake, and concomitant medications. For GTN-exposed participants, details regarding duration of GTN use, frequency of application, and self-

reported adherence were documented. Resting anal canal pressure was measured using standardized anorectal manometry performed by trained personnel, following established clinical protocols. Maximum resting pressure (mmHg) was recorded as the primary physiological outcome. To ensure measurement reliability, the same manometry equipment was used where feasible, and calibration procedures were verified prior to data collection sessions. Symptom severity was assessed using a structured composite symptom score capturing key haemorrhoidal symptoms, including pain intensity (measured using a visual analogue scale), frequency of rectal bleeding, pruritus or irritation, and difficulty during bowel movements. Higher composite scores indicated greater symptom burden. Internal consistency of the symptom composite was evaluated using Cronbach's alpha. Haemorrhoid grading was independently verified in a subset of participants to assess inter-rater agreement. Data were analyzed using Social Package for statistical software. Continuous variables were summarized as mean ± standard deviation for normally distributed data and median with interquartile range for non-normally distributed data. Categorical variables were expressed as frequencies and percentages. Normality was assessed using the Shapiro–Wilk test. Between-group comparisons were performed using independent-samples t-tests for parametric data and Mann–Whitney U tests for non-parametric data. Associations between resting anal canal pressure and symptom severity were assessed using Pearson correlation for normally distributed variables or Spearman's rank correlation for non-parametric data. Multivariable linear regression analyses were conducted to adjust for potential confounders, including age, sex, haemorrhoid grade, constipation severity, and stool consistency. Statistical significance was defined as a two-tailed p-value of less than 0.05. All study procedures were conducted in accordance with the Declaration of Helsinki. Confidentiality was maintained using anonymized study codes, and participants were free to withdraw from the study at any time without impact on their clinical care.

Results

A total of 142 patients with symptomatic internal haemorrhoids were included in the final analysis. Of these, 72 patients had been using topical glyceryl trinitrate (GTN) 0.2% ointment for at least seven days (GTN-exposed group), while 70 patients were receiving conservative non-GTN management (non-exposed group). All participants completed symptom assessment, and resting anal canal pressure measurements were successfully obtained in all cases.

Table:1 *Baseline Demographic and Clinical Characteristics of Participants*

Variable	GTN-Exposed (n = 72)	Non-Exposed (n = 70)	p-value	Variable
Age (years), mean ± SD	42.6 ± 11.3	44.1 ± 10.8	0.41	Age (years), mean ± SD
Male, n (%)	41 (56.9)	38 (54.3)	0.76	Male, n (%)

BMI (kg/m²), mean ± SD	26.1 ± 3.8	26.4 ± 3.6	0.58	BMI (kg/m²), mean ± SD
Goligher grade I–II, n (%)	49 (68.1)	46 (65.7)	0.75	Goligher grade I–II, n (%)
Goligher grade III, n (%)	23 (31.9)	24 (34.3)	0.75	Goligher grade III, n (%)
Constipation history, n (%)	44 (61.1)	47 (67.1)	0.45	Constipation history, n (%)

There were no statistically significant differences between groups with respect to age, sex, body mass index, haemorrhoid grade, or constipation history, indicating baseline comparability.

Table 2: *Resting Anal Canal Pressure and Symptom Scores by Exposure Status*

Outcome	GTN-Exposed	Non-Exposed	p-value
Resting anal pressure (mmHg), mean ± SD	92.8 ± 28.6	113.9 ± 34.2	<0.001
Pain score (VAS), mean ± SD	3.1 ± 1.4	4.6 ± 1.7	<0.001
Bleeding frequency score, median (IQR)	1 (1–2)	2 (1–3)	0.003
Composite symptom score, mean ± SD	8.9 ± 3.2	12.4 ± 3.8	<0.001

Patients using topical GTN demonstrated significantly lower resting anal canal pressures and reduced symptom severity across multiple domains compared with non-exposed patients.

Table 3: *Correlation Between Resting Anal Canal Pressure and Symptom Severity*

Symptom Measure	Correlation Coefficient (r)	p-value
Pain score (VAS)	0.54	<0.001
Bleeding frequency	0.38	<0.001
Composite symptom score	0.59	<0.001

Higher resting anal canal pressures were significantly associated with increased pain intensity, bleeding frequency, and overall symptom burden.

Table 4: *Multivariable Linear Regression Analysis for Factors Associated With Composite Symptom Score*

Variable	β (Standardized)	95% CI

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GTN use (yes vs no)	−0.42	−2.9 to −1.6
Resting anal pressure (mmHg)	0.36	0.02 to 0.05
Haemorrhoid grade (III vs I–II)	0.21	0.6 to 1.9
Constipation history	0.17	0.4 to 1.6

After adjustment for potential confounders, GTN use remained independently associated with lower symptom severity, while higher resting anal canal pressure and advanced haemorrhoid grade were associated with increased symptom burden

Discussion

In this cross-sectional observational study, topical glyceryl trinitrate (GTN) 0.2% use was associated with lower resting anal canal pressure and reduced haemorrhoidal symptom burden compared with non-exposed patients managed conservatively. The findings are in line with the clinical manometry study by Tjandra et al. (2007), in which author investigated haemorrhoid symptoms in the context of elevated resting pressures and reported a significant reduction in maximum resting anal canal pressure following Rectogesic® 0.2% (mean 115.0 ± 40.4 mmHg to 94.7 ± 34.1 mmHg, $P < 0.001$). It was accompanied by significant improvements in bleeding, pain, pruritus, irritation, and difficulty with bowel movement; headache was the most frequent adverse event (reported in 43.1%). The direction and magnitude of association in our cohort (lower resting pressure and improved multi-symptom burden among GTN users) are consistent with those outcomes, despite differences in design: the earlier work used a more explicitly treatment-follow-up framework, whereas our analysis reflects real-world exposure status at assessment[7]. Notably, our regression model indicated that both resting pressure and haemorrhoid grade were independently associated with symptom burden, suggesting that GTN's benefit may be most clinically relevant in patients where hypertonia contributes substantially to symptom expression which are also consistent with the rationale for selecting haemorrhoid patients with high resting pressures in the Tjandra study[7]. The observed relationship of pressure symptom is mechanistically plausible. This pharmacodynamic principle is reflected in official product descriptions for rectal GTN, which describe reduced anal pressure following topical application[10]. Experimental manometry data also support a rapid but time-limited reduction in maximal resting pressure after topical 0.2% GTN, with significant decreases observed within 15–90 minutes post-application and recovery thereafter highlighting why adherence and timing relative to assessment can influence measured associations. From an observational standpoint, this emphasizes the importance of documenting dosing interval prior to manometry, as "recent application" may yield lower measured pressures than delayed assessment[11]. Although postoperative haemorrhoidectomy pain is not identical to non-surgical haemorrhoid symptomatology, the haemorrhoidectomy literature provides convergent evidence that GTN can reduce anorectal pain, plausibly via sphincter relaxation and reduced spasm. A randomized, double-blind, placebo-controlled study reported improved postoperative pain and wound healing outcomes with topical

GTN after haemorrhoidectomy[12]. Meta-analytic evidence similarly concludes that GTN ointment confers significant analgesic benefit during the intermediate postoperative period (days 3–7) and may improve wound healing outcomes, while acknowledging heterogeneity and small trial sizes[13]. A later meta-analysis of randomized trials also evaluated topical GTN for post-haemorrhoidectomy pain relief, supporting an analgesic effect, though pooled effects vary with protocol and outcome timing[14]. These surgical findings, taken together with our outpatient symptom associations, reinforce GTN's clinical relevance to anorectal pain states where sphincter hypertonia is contributory even though generalization from postoperative cohorts to non-surgical haemorrhoids should remain cautious. Our study provides context-specific evidence in a population that may differ from earlier studies in diet, constipation prevalence, health-seeking behavior, and medication access patterns—factors that can modulate haemorrhoid symptoms and response to conservative care[15]. The use of anorectal manometry as the physiological anchor strengthens interpretability, as manometry is the established method for characterizing sphincter function and defecatory coordination[16]. However, haemorrhoid pathophysiology is multifactorial; hypertonia may be one contributor among venous factors, connective tissue support, and defecatory mechanics[17]. Studies evaluating pressure patterns across anorectal disorders illustrate that elevated resting pressure is a meaningful physiological phenotype in certain anorectal conditions, though its role in haemorrhoids is debated[18]. Accordingly, our findings are best interpreted as supporting a *pressure-linked symptom subgroup* for which GTN may be particularly relevant, rather than implying that all haemorrhoid symptoms are driven by high resting tone[19,20].

Limitations of the Study

A key strength of this study is the coupling of patient-reported symptom burden with objective physiological measurement (resting anal pressure) in a routine-care setting. The age range and exclusion criteria helped reduce confounding from conditions where GTN is more directly indicated (e.g., fissure as the primary diagnosis) and from contraindicated medication combinations[21-23]. Nevertheless, limitations intrinsic to cross-sectional observational design remain. Causality cannot be inferred, and confounding by indication is possible (e.g., clinicians may preferentially prescribe GTN to patients perceived to have spasm-related pain). Timing of last GTN application relative to manometry may have introduced measurement variability, given the documented short-term pressure-lowering profile of topical GTN[24]. Self-reported adherence may be influenced by tolerability, particularly headache—a common adverse effect reported in haemorrhoid-associated GTN use. Future studies would benefit from prospective measurement of dosing timing, standardized symptom instruments validated for haemorrhoids, and propensity-score approaches to reduce confounding.

Conclusion

Topical glyceryl trinitrate (0.2%) use was associated with lower resting anal canal pressure and reduced symptom severity in patients with symptomatic haemorrhoids. These findings support

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GTN as a potential adjunctive pharmacological option in haemorrhoid patients with pressure-related symptomatology, warranting further prospective evaluation.

Author Contributions:

Ms Noor Us Saba Nadeem verifies the full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis

Concept and design: Noor Us Saba Nadeem

Acquisition, analysis, or interpretation of data: Noor Us Saba Nadeem

Drafting of the manuscript: Noor Us Saba Nadeem

Critical review of the manuscript for important intellectual content: Noor Us Saba Nadeem

Statistical analysis: Noor Us Saba Nadeem

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