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Comparative Study of Placebo Versus Metronidazole as a Role of Pain Relief Post Hemorrhoidectomy

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ABSTRACT

Objective: To assess the role of metronidazole versus placebo in terms of pain relief post hemorrhoidectomy.

Methodology: This randomized control trial was done at the general surgery department of PUMHS from January 2022 to July 2022. The study included adult patients of both genders, aged 18-60, who underwent surgeries for grade III and grade IV hemorrhoids. The participants were divided into two groups: a control group and an intervention group that received oral metronidazole for seven days postoperatively. Both groups received a standardized post-operative analgesic treatment. Post-operative pain and its severity were assessed using the Visual Analog Scale (VAS). Data were collected using a study proforma, and statistical analysis was performed using SPSS version 26.

Results: A total of 60 cases of hemorrhoids were comparatively studied; mean age of the case group was 39.36+10.43 years and the mean age of the control group was 35.33+9.35 years (p=0.120). The mean BMI and average disease duration was statistically insignificant according to both groups (p > 0.05). In the cases group, grade III hemorrhoids were 36.7% and grade IV hemorrhoids were 63.3%, while in the control group, grade III hemorrhoids were 46.7% and grade IV hemorrhoids were 53.3% (p=0121). The mean operative time was almost similar in both groups (p=0.515). Average VAS was significantly decreased in the case group after 2 hours, at 24 hours, at 36 hours, and at 48 hours (p=<0.05), while it was statistically insignificant according to both groups at the 7th post-operative day (p=0.091).

Conclusion: The use of oral or topical metronidazole in the post-operative period concludes to be more effective in terms of clinically significant early pain relief.

Key words: Hemorrhoids, grade III, grade IV, pain.

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Introduction

Hemorrhoidal disease is a prevalent non-malignant condition with significant medical and socio-economic implications.[1] Hemorrhoids, characterized by swollen veins in the rectum or anus, can lead to discomfort, pain, itching, and bleeding. The condition encompasses internal hemorrhoids located within the rectum and external hemorrhoids situated outside the anus. Several factors contribute to hemorrhoid development, including constipation, pregnancy, lack of physical activity, obesity, and aging.[2]

While hemorrhoids are generally not a severe medical condition, they can cause significant discomfort and may necessitate various non-surgical and surgical interventions for treatment. Surgical intervention is typically recommended for grade IV hemorrhoids, strangulated internal hemorrhoids, symptomatic grade III hemorrhoids, and thrombosed hemorrhoids.[3]

Postoperative pain is a common issue associated with hemorrhoidectomy, which may be caused by the contraction of the internal anal sphincter.[4,5] The sensation of pain arises due to both internal and external factors

affecting the peripheral nerve endings, as well as abnormal activation of the central nervous system.[6] When undergoing surgery, nociceptors are triggered by a variety of stimuli, including mechanical factors such as cutting or puncturing of tissues, chemical factors from exposure to inflammatory mediators, and thermal factors from heating or cooling of the tissues.[6,7] As a result, surgery always induces some level of pain with varying degrees of intensity. Various methods have been utilized to alleviate this discomfort, such as applying topical treatments like 0.2% and 0.4% Glyceryl Trinitrate (GTN), 2% 3,4 Lignocaine gel, and metronidazole.[4,8] Metronidazole has been acknowledged for its ability to alleviate pain following a hemorrhoidectomy when administered through the systemic route.[9] The reason behind its effectiveness in reducing post-operative pain after a hemorrhoidectomy is attributed to its antimicrobial properties that lead to decreased bacterial colonization at the surgical sites, as well as its anti-inflammatory effects.[9] Some studies showed that the after hemorrhoidectomy, metronidazole is considered effective for pain management.[9-11] However, there is a need for comparative studies to determine the true efficacy of metronidazole for pain relief after hemorrhoidectomy. A comparative study of placebo versus metronidazole in the context of pain relief post-hemorrhoidectomy would help to determine whether metronidazole is truly effective in reducing pain levels. By comparing the pain scores of patients who receive metronidazole with those who receive a placebo, researchers can determine whether metronidazole provides significant pain relief beyond the placebo effect.

Methodology

This randomized controlled trial was conducted at the General Surgery Department of Dow University Hospital in Karachi from January 2022 to July 2022. The inclusion criteria consisted of patients aged 18 to 60 years, both gender, who underwent surgeries for grade III and grade IV hemorrhoids, and those who were willing and able to provide informed consent to participate in the study. On the other hand, patients with a history of allergic reactions to metronidazole or any other nitroimidazole antibiotic, those patients' with a history of significant gastrointestinal diseases such as inflammatory bowel disease or diverticular disease, individuals with a history of bleeding disorders or those currently taking anticoagulant medications, those with a history of chronic pain or regular use of pain medications, as well as patients with a history of drug or alcohol abuse were excluded from the study.

The allocation of patients to the two groups was done randomly to ensure that there was no selection bias. One group served as the control group and received a placebo, while the second group received oral metronidazole post-operatively for seven days. The study participants were given information about the research and were required to provide written consent before participating in the study. The patients were followed up for seven days after the surgery, during which their pain levels were assessed at different time intervals using a visual analog scale or other validated pain assessment tools. The pain scores of the two groups were then compared to determine the efficacy of metronidazole in pain relief post-hemorrhoidectomy. All the information was collected via study proforma and SPSS version 26 was used for the data analysis.

Results

A total of 60 cases of hemorrhoids (grade III and IV) were comparatively studied; mean age of cases group was 39.36±10.43 years and mean age of control group was 35.33±9.35 years (p=0.120). Mean BMI in case group was 24.60±4.37 kg/m^2 and mean BMI in control group was 24.26±3.78 kg/m^2. Average of disease duration in group A was 2.50±1.45 years and average of disease duration in group B was 1.92±1.22 years (p=0.199). Table I

Table I: Descriptive statistics of age, BMI and duration of disease (n=60)

Variables	Study groups	N	Mean	SD	p-value
Age	**Cases group**	30	39.36	10.43	
	Control group	30	35.33	9.35	0.120
BMI	**Cases group**	30	24.60	4.37	
	Control group	30	24.16	3.78	0.683
Duration of disease	**Cases group**	30	2.50	1.45	
	Control group	30	1.92	1.22	0.199

According to the grads of hemorrhoids in cases group grade III was 36.7% and grade IV 63.3%, while in control group grade III hemorrhoids was 46.7% and grade IV was 53.3%, findings were statistically insignificant (p=0121). Table II

Mean operative time in case group was 39.50±8.45 minutes and in control group was 38.30+5.38 minutes (p=0.515). Average VAS was significantly decreased in cases after 2 hours, at 24 hours, at 36 hours and at 48 hours (p=<0.05), while average VAS was statistically

insignificant according to both groups (p=0.091). Table III

Table II: Grade of hemorrhoids in the both groups(n=60)

Variables		Study groups: Cases group	Study groups: Control group	Total	p-value
Grade of hemorrhoids	**3rd degree**	11	17	28	0.121
		36.7%	56.7%	46.7%	
	4th degree	19	13	32	
		63.3%	43.3%	53.3%	
Total		30	30	60	
		100.0%	100.0%	100.0%	

Table III: Comparison of pain in the both study groups (n=60)

Outcomes	Study groups	N	Mean	SD	p-value
Operative time (minutes)	Cases group	30	39.50	8.45	0.515
	Control group	30	38.30	5.38	
Pain (VAS) score (after 2 hours)	Cases group	30	3.30	2.03	0.030
	Control group	30	4.33	1.51	
Pain (VAS) score (after 24 hours)	Cases group	30	2.33	1.74	0.015
	Control group	30	3.40	1.54	
Pain (VAS) score (after 36 hours)	Cases group	30	1.50	1.54	0.015
	Control group	30	2.56	1.73	
Pain (VAS) score (after 48 hours)	Cases group	30	0.80	1.15	0.026
	Control group	30	1.80	2.10	
Hospital stays (On 7th day)	Cases group	30	0.43	0.77	0.091
	Control group	30	1.03	1.75	

Discussion

Hemorrhoids are a prevalent condition characterized by swollen or inflamed veins in the anus or rectum, classified into four degrees of severity. This study aimed to compare the metronidazole with those who receive a placebo in terms of pain relief. The study included participants with a mean age of 37.35±10.03 years, with females comprising the majority at 53.3% and males were 46.7%.

In the comparison of this study, Ali MT et al[12] reported that, mean age of the patients was 41.2±3.2 years, while inconsistently they found males in majority. On the other hand, Aljabery RMS et al[13], reported the mean age of their subjects was 38.9 years, with they also found males in majority 66.66% and females 33.44%. Another study by Baig AA et al[14] reported that the average age of their subjects was 41.54±6.380 years, with males being the most common at 61.3% and females at 38.7%. Although the exact cause of male predominance in hemorrhoids is not well understood, lifestyle factors like diet, obesity, and lack of physical activity may play a role, and occupational hazards like long periods of sitting or heavy lifting may also contribute to the development of hemorrhoids. According to this study slightly higher rate of hemorrhoids in women compared to men, which may be attributed to factors like pregnancy, childbirth, and hormonal changes.

In our study, the average Visual Analog Scale (VAS) scores were significantly lower in the case group at 2 hours, 24 hours, 36 hours, and 48 hours after the operation (p=<0.05). Similarly, Di Re A et al. 15 observed a significant decrease in VAS scores at all-time points, with the most substantial reduction observed on the 5th day following hemorrhoidectomy.

In contrast, Neogi P et al.[11] reported that the groups receiving metronidazole demonstrated significantly better pain relief on post-operative days 1, 3, and 7, as evidenced by the lower requirement for analgesics in these patients. In line with these findings, González-Ojeda A et al.[16] observed that oral administration of metronidazole was an effective intervention for pain control following closed hemorrhoidectomy. These findings suggest that initiating analgesic treatment can reduce postoperative pain during defecation, and the group receiving metronidazole was able to resume daily activities earlier.[17] Our findings supported by Rehman S et al. [17] and Mohammed MK et al.[18], who reported that metronidazole is an effective intervention for early pain control after closed hemorrhoidectomy.

Several studies have reported that the use of metronidazole resulted in significantly better pain relief on postoperative days 0, 1, 3 and 7 compared to control groups. This suggests that metronidazole may be a useful option for managing postoperative pain after hemorrhoidectomy. Additionally, patients who received metronidazole reported using fewer analgesics, and were able to resume their daily activities earlier than those in the control group. Overall, the use of metronidazole appears to be a promising approach for improving pain management and patient outcomes following hemorrhoidectomy.

However, it is important to consider several limitations in the study of metronidazole's role in post-hemorrhoidectomy pain relief. One primary limitation is the small sample size, which may have restricted the statistical power of the study and the generalizability of the findings to larger populations. Further studies with larger sample sizes, prospective designs, and placebo-controlled trials are necessary to confirm the efficacy of metronidazole as a pain relief treatment for post-hemorrhoidectomy.

Conclusion

The use of metronidazole as a therapeutic intervention for pain relief post-hemorrhoidectomy has shown promising results. It has demonstrated effectiveness as an initial analgesic treatment, facilitating a reduction in postoperative pain during defecation and promoting earlier resumption of daily activities for patients.

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