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Comparative Study Between Oral and Topical Metronidazole in Early Recovery from Pain After Open Haemorrhoidectomy

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Abstract: ***Study Design: Single blind randomized controlled study. Study Place: Department of General Surgery, Raipur institute of medical sciences, Raipur - Chhattisgarh. Study Period: study will be conducted in year of 2022-2024 (18 months) in the department of General surgery. Data Collection: Interview and questionnaire method Study Population: This study will be done in 90 patients divided into oral and topical group with each group receiving 50 gm diclofenac as base analgesic.Patients in the primary group will receive per Topical metronidazole 400mg TDS and secondary group will receive oinment metronidazole 2% local application TDS. Pain will be assessed using Visual analogue scale at 6,12, 24 , 48,72 hrs. Results: From the study of 90 patients (45 in each groups) it was found that topical metronidazole group had early recovery and experienced less pain as compared to oral metronidazole group. Descriptive statistics analysis, frequency analysis, percentage analysis, were used to categorical variables and mean and S.D were used for continuous variables. Conclusion: 1) Topical metronidazole has a favourable effect in pain control in the post hemorrhoidectomy patients in addition to antimicrobial effect as compared to oral metronidazole. 2) Topical metronidazole as overall causes better patient satisfaction and earlier recovery and less post operative pain following open haemorrhoidectomy.***

Keywords: Oral Metroidazole, Topical Metronidazole, Haemorrhoidectomy, Pain control, Patient recovery

1. Introduction

Haemorrhoids are one of the most common anorectal diseases for referral to a surgeon. Haemorrhoidectomy one of the most common anorectal procedures performed. Complaints pertaining to haemorrhoids are one of the most common afflictions of western civilizations. Although the condition is rarely life threatening the complications of therapy can be.[1]

The Indian Susruta Samhita, an ancient Sanskrit text dated between the fourth and fifth century AD, described treatment procedures comparable to those in the Hippocratic treatise, but with advancement in surgical procedures and emphasis on wound cleanliness.[2]

For haemorrhoids of grade III AND IV the effective treatment even today remains to be hemorrhoidectomy. Milligan Morgan described conventional open hemorrhoidectomy in 1937 and Ferguson in 1959 described closed hemorrhoidectomy. Owing to low expense and technical ease open hemorrhoidectomy is the procedure of choice, even though newer modalities have come in to play.

Hemorrhoids not responding to non-operative management, recurrent after banding and sclerotherapy and 3rd and 4th degree are treated surgically by hemorrhoidectomy, stapler hemorrhoidopexy.

Many different interventions have been described which attempt to reduce post operative pain: these include infiltration of local anaesthetic, pre operative laxatives and administration of nitro-glycerine ointment with varying degrees of success. Perhaps the most widely used pharmacological intervention following haemorrhoidectomy is the use of prophylactic antibiotics, particularly metronidazole, administered either systemically or topically.

Metronidazole offers good protection from anaerobic, enteric commensals that could infect the wounds and, in addition, potentially promotes wound healing as a consequence of its antioxidant effects. Whilst metronidazole is used to reduce post operative pain, there is a lack of consensus as to its effectiveness with studies of variable quality and design demonstrating conflicting results.[3]

The investigators in this study evaluated the effect of topical administration versus oral administration of metronidazole and diclofenac as a base analgesic in pain control after hemorrhoidectomy.

Post-operative complications such as pain, bleeding, non-healing wounds, incontinence, stenosis, and urinary retention. Pain is the major post-operative complaint and is attributed to surgical wounds in sensitive anoderm, edema, spasm, and infection. Various remedies have been suggested to alleviate post- operative pain like GTN 0.2%, topical NSAIDs, Ca channel blockers, and metronidazole. Studies show that metronidazole significantly reduces the post-operative pain and improves wound healing.

The investigators in this trial will re-examine the efficacy of metronidazole in oral versus topical form with standardized analgesic usage. This will be a biosimilar clinical trial.

2. Materials and Method

Study Design: Single blind randomized controlled study.

Study Place: Department of General Surgery, Raipur

institute of medical sciences, Raipur – Chhattisgarh.

Study Period: study will be conducted in year of 2022-2024 (18 months) in the department of General surgery.

Data Collection: Interview and questionare method

Study Population:

This study will be done in 90 patients divided into oral and topical group with each group receiving 50 gm diclofenac as base analgesic.Patients in the primary group will receive per Topical metronidazole 400mg TDS and secondary group will receive oinment metronidazole 2% local application TDS.Pain will be assessed using Visual analogue scale at 6,12, 24, 48,72 hrs.

Inclusion Criteria

All the patients attending surgery outpatient department with the complaints bleeding per rectum and diagnosed to have hemorrhoidal disease grade 2, grade 3 and grade 4 hemorrhoid patients above 18 years of age.

Exclusion Criterion

Patients below 18 years of age Pregnancy
Lactation Fissure in Ano Fistula in Ano
Previous anorectal disease Hypersensitivity to metronidazole Coagulation disorder Haemoglobin <8g/dl
Malignant Hypertension Anesthetically unfit patients Malignancy

Sampling Technique:

Block Random sampling - The study will be done in 90 patients of grade 2 ,grade 3 and grade 4 of haemorrhoids of either sex above 18 years of age (metronidazole oral and topical). Patients will be divided into two groups of 45 each by using Block Randomization manner and will chart using 4 columns like **D1D1D2D2, D2D2D1D1, D1D2D1D2, D2D1D2D1** respectively where D1 stands for TOPICAL metronidazole and D2 stands for ORAL metronidazole.

Group D1 (n=45) Group D2(n=45).
In master chart TOPICAL metronidazole is D1 and ORAL metronidazole is group D2

Statistical Analysis: Continuous variables will be presented as mean ± SD, and categorical variables will be presented as absolute numbers and percentages. Data will be checked for normality by the Kolmogorov-Smirnov test before the statistical analysis. Normally distributed continuous variables will be compared using the unpaired t-test, whereas the Mann-Whitney U test will be used for those variables that will not be normally distributed. Categorical variables will be analyzed using either the chi-square test or Fisher's exact test. A p-value of <0.05 will be considered statistically significant. The data will be considered in MS excel spread sheet and analysis will be done with Statistical package for social sciences SSPS.

3. Observations and Results

This is a randomized control study, conducted in the department of General Surgery, Raipur institute of medical sciences, Raipur – Chhattisgarh, Main aim this study is ‘‘To compare the analgesic effect of oral and topical application of metronidazole in post operative open hemorrhoidectomy’’. In this study we found these results-

Demographic Differences:

[1] The demographic composition of the two groups differed, with the topical metronidazole group (D1) having 31.1% males, while the oral metronidazole group (D2) had a higher male composition of 38.8%. For topical metronidazole, 17 females (18.8%) and 28 males (31.1%) received the drug. For oral metronidazole, 10 females (10%) and 35 males (35%) received the drug.

Table 1: Distribution by gender

Sex	Drug Given				Chi-square	P
	Topical metronidazole		Oral metronidazole			
	Frequency	%	Frequency	%		
F	17	18.8	10	11.11	1.9048	0.1675
M	28	31.1	35	38.88		

The frequencies of oral and topical metronidazole administration were compared between males and females. The chi-square test was used to determine if there was a significant association between sex and the type of drug given. With a p-value of 0.1675, which is greater than the conventional significance level of 0.05, we fail to reject the null hypothesis. Therefore, we conclude that there is no significant difference in the frequency of drug administration between males and females.

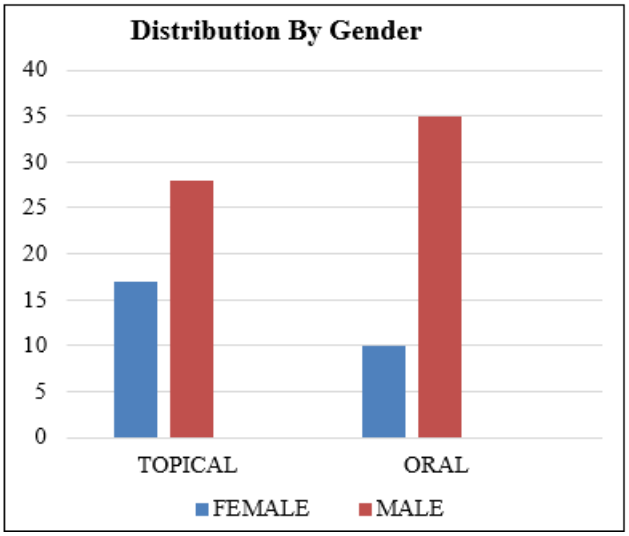


Table 2: Distribution by age group

Age Group	Drug Given				Chi-square	P value
	Topical Metronidazole		Oral Metronidazole			
	Frequency	%	Frequency	%		
20-30 yrs	4	4.35	5	5.43	20.482	0.08
31-40 yrs	7	7.61	4	3.26		
41-50 yrs	10	10.9	10	9.78		
51-60 yrs	12	13.0	12	13.0		
61-70 yrs	6	5.43	11	12.0		
71-80 yrs	5	1.09	5	5.43		
81-90 yrs	1	5.43	0	0		

The frequencies of oral and topical metronidazole

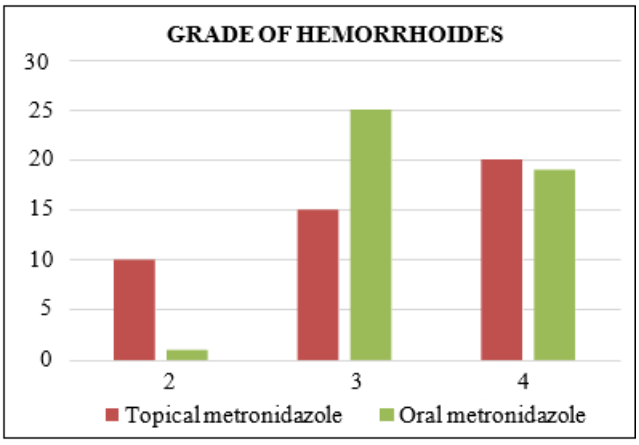
administration were compared across different age groups. The chi-square test was used to determine if there was a significant association between age group and the type of drug given. With a p-value of 0.08, which is slightly higher than the conventional significance level of 0.05, we fail to reject the null hypothesis. Therefore, we conclude that there is no significant difference in the frequency of drug administration across different age groups.

[1] For topical metronidazole, frequencies ranged from 1 (81-90 years) to 12 (51-60 years) individuals, while for oral metronidazole, frequencies ranged from 0 (81-90 years) to 12 (51-60 years) individuals. there is no significant difference in the frequency of drug administration across different age groups. Maximum patient ranged in age group between 40-60 years of age group in both topical and oral metronidazole group.

Table 3: Grade of hemorrhoids

Grade of Hemorrhoids	Total	Topical Metronidazole [D1]	Oral metronidazole [D2]	P= 0.007
2	11 (12%)	10 (22%)	1 (2.2%)	
3	40 (44%)	15 (33%)	25 (56%)	
4	39 (43%)	20 (44%)	19 (42%)	

The distribution of participants across different grades is significantly different between the two groups (p = 0.007). In group D1, there is a higher proportion of grade 2 participants (2.2%) compared to D2 (22%). while in group D2 have high proportion of grade-3 participants [56%] compared to D1 [33%], but approximately same proportion of participants in grade -4 in both topical and oral metronidazole group. P value is significant for the grade of hemorrhoids for both groups.



In our study large number patients were of grade 3 haemorrhoid comprised of 15 patients in topical group and 25 patients in oral group followed by grade4 and then grade 2.

Table 4: Post hemorrhoidectomy pain

Time Points	Drug Given				P Value
	Topical Metronidazole		Oral Metronidazole		
	Mean	SD	Mean	SD	
Baseline	0.288	0.54	0.71	0.89	0.034
6 Hours	5.511	1.8	7.7	0.09	0.04
12 Hours	4.4	1.6	7.2	1.09	0.036
24 Hours	6.4	3.6	6.2	1.15	0.01
72 Hours	3.04	O.8	6	1.6	0.017

Post-hemorrhoidectomy pain assessment-

[4] The post hemorrhoidectomy pain was assessed using visual analogue scale (VAS) immediately after the surgery, after 6 hours, after 12 hours, at day1 and at day3. The mean VAS score between Group D1 (Topical Metronidazole group) and Group D2 (oral metronidazole) which were all statistically significant when compared after 6hours [p=0.04], after 12 hours [p=0.036], at day1 [p=0.01] and at day 3 [p=0.017]. With the above-mentioned observations, we inferred that topical metronidazole showed a better pain control when compare to the oral metronidazole.

At 6 hour-

At 6 hours, the mean values for topical metronidazole and oral metronidazole were 5.511 and 7.7, respectively, with standard deviations of 1.8 and 0.09. The p-value for this comparison was 0.04, suggesting a significant difference between the two groups at 6 hours.

At 12- hours-

At 12 hours, the mean values for topical metronidazole and oral metronidazole were 4.4 and 7.2, respectively, with standard deviations of 1.6 and 1.09. The p-value for this comparison was 0.036, suggesting a significant difference between the two groups at 12 hours.

At 24- hours-

At 24 hours, the mean values for topical metronidazole and oral metronidazole were 6.4 and 6.2, respectively, with standard deviations of 3.6 and 1.15. The p-value for this comparison was 0.01, suggesting a significant difference between the two groups at 24 hours.

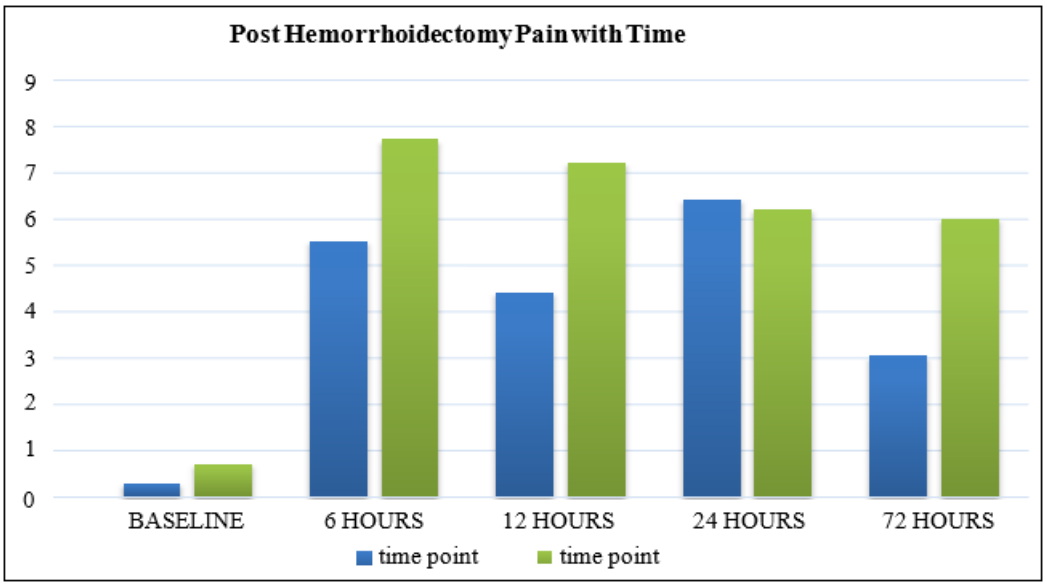
At 72 hours-

At 72 hours, the mean values for topical metronidazole and oral metronidazole were 3.04 and 6.0, respectively, with standard deviations of 0.8 and 1.6. The p-value for this comparison was 0.017, suggesting a significant difference between the two groups at 72 hours.

These findings suggest that the efficacy or response to treatment varies significantly between oral and topical metronidazole at different time points, with one drug type showing superior effectiveness over the other at various stages of treatment.

The median baseline VAS score is 0.00 for both groups, indicating that participants in both groups reported no baseline pain on average. However, there is a statistically significant difference between the groups (p = 0.015), suggesting that even though the difference is small, it's still noteworthy.

6-hour, 12-hour, 24-hour, and 72-hour VAS scores: There are significant differences in pain levels between the two groups at 6 hours ($p < 0.001$), 12 hours ($p < 0.001$), 24 hours ($p < 0.001$), and 72 hours ($p < 0.001$) post-treatment. Participants in group D1 [topical metronidazole] consistently report lower pain levels compared to those in group D2 [oral metronidazole] across all time intervals.



Graph 4: Post hemorrhoidectomy pain with time

Table 5: Post-defecation pain

Post Defecation Pain	Drug Given				P Value
	Topical Metronidazole		Oral Metronidazole		
	Number	Percentages	Number	Percentages	
	6	14	3	6.8	0.31

Table 6: Duration to Return to Normal Activity

Return to Normal Activity	Drug Given				P Value
	Topical Metronidazole		Oral Metronidazole		
	Mean	SD	Mean	SD	
	9.066	1.21	11.22	1.3	0.034

Post-defecation pain-

There are 6 patients [14%] have post defecation pain in topical metronidazole group while 3 patients [6.8%] have found in oral metronidazole group. There's no significant difference in post-defecation pain between the two groups (p = 0.31). This suggests that regardless of the treatment group, participants experience similar levels of pain after defecation.

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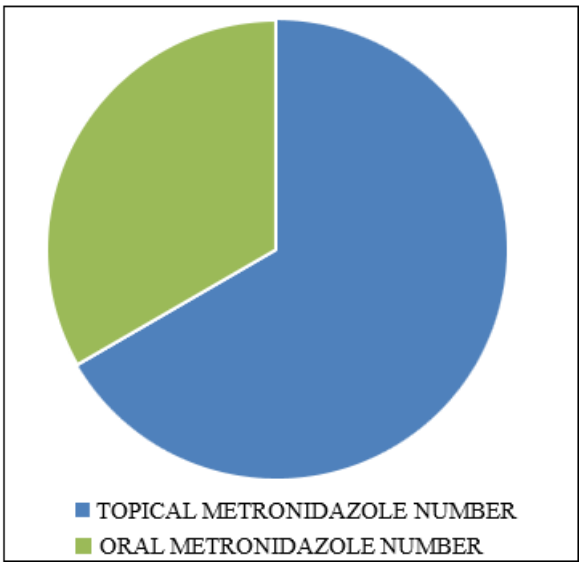

Duration to Return to Normal Activity:

[6] The mean return to normal activity after treatment with topical metronidazole was 9.066, with a standard deviation of 1.21. For oral metronidazole, the mean was 11.22, with a standard deviation of 1.3. there is a significant difference in the efficacy of topical metronidazole compared to oral metronidazole in facilitating the return to normal activity after treatment. Specifically, topical metronidazole appears to be more effective in this regard compared to oral administration.

The p-value associated with this comparison was 0.034, indicating a statistically significant difference in the return to normal activity between the two treatment groups.

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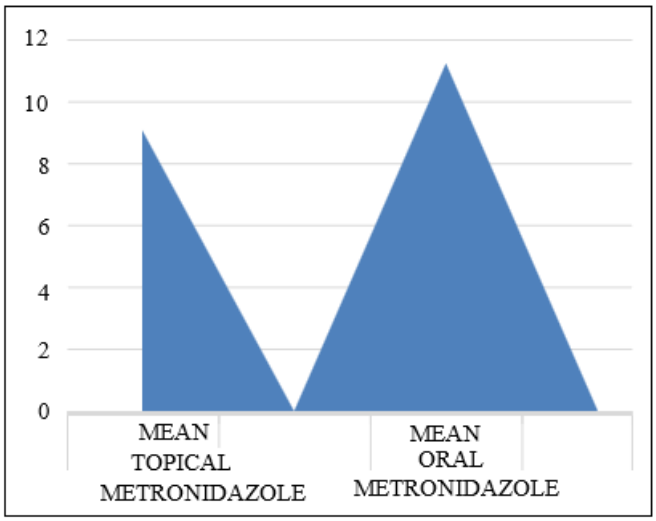

Graph 6: Duration of Return of normal activity

Graph depicting mean days in both the group in relation to return to normal activity.

4. Discussion

Post-Hemorrhoidectomy Pain Assessment-

The post hemorrhoidectomy pain was assessed using visual analogue scale (VAS) immediately after the surgery, after 6 hours, after 12 hours, at day1 and at day3. The mean VAS score between Group D1 (Topical Metronidazole group) and Group D2 (oral metronidazole) which were all statistically significant when compared after 6hours [p=0.04], after 12 hours [p=0.036], at day1 [p=0.01] and at day 3 [p=0.017]. With the above-mentioned observations, we inferred that topical metronidazole showed a better pain control when compare to the oral metronidazole. The median baseline VAS score is 0.00 for both groups, indicating that participants in both groups reported no baseline pain on average. 6-hour, 12-hour, 24-hour, and 72-hour VAS scores: There are significant differences in pain levels between the two groups at 6 hours ($p < 0.001$), 12 hours ($p < 0.001$), 24 hours ($p < 0.001$), and 72 hours ($p < 0.001$) post-treatment. Participants in group D1 [topical metronidazole] consistently report lower pain levels compared to those in group D2 [oral metronidazole] across all time intervals.

A study done by **Thomas J Nicholson** et al, 2004 did prospective randomized controlled trial and in this study, it was found that patients in the topical metronidazole group experienced less post operative pain. [P=0.02]. [4]

Sergio Solorio lopez et al 2015 also found that Metronidazole was effective in pain management after hemorrhoidectomy in comparison to the placebo with less need of rescue analgesia. [P<0.05].[5]

Study done by **Abbas et al**., titled "Comparison of mean pain score using topical and oral metronidazole in post Milligan Morgan hemorrhoidectomy patient; A randomized controlled trial" conducted at the Akbar Niazi Teaching Hospital in Islamabad aimed to assess postoperative pain in patients undergoing Milligan Morgan Hemorrhoidectomy. The prospective randomized controlled trial included 166 patients with 3rd and 4th degree hemorrhoids. The patients were divided into two groups, one receiving topical metronidazole and the other oral metronidazole, for seven days post-surgery. Pain scores were recorded using the Visual Analog Scale (VAS) on the 1st and 7th postoperative days. The results indicated a significantly lower pain score in patients using topical metronidazole compared to oral metronidazole. The study found no significant association between pain and patient age, while a significant difference was observed between genders. The findings suggest that topical metronidazole may be more effective in reducing post-hemorrhoidectomy pain compared to the oral form.[6]

Neogi P et al, had done a prospective randomized controlled trial being conducted on 67 patients attending the Surgical OPD at SRN Hospital, at Allahabad in 2017

Mohammed et al., revealed significant findings regarding the impact of oral Metronidazole therapy on postoperative pain after open "Morgan-Milligan" hemorrhoidectomy. The study included 64 adult patients, The patients who received Metronidazole exhibited lower mean Visual Analogue Scale (VAS) scores on the 1st, 3rd, 7th day, and during the first bowel motion compared to the control group. These results suggest that oral Metronidazole therapy may play a role in reducing pain intensity and improving overall recovery outcomes in patients undergoing open hemorrhoidectomy.[7]

Ala et al., aimed to evaluate the efficacy of topical metronidazole (10 percent) in alleviating postoperative and after-defecation pain following hemorrhoidectomy. The results demonstrated that patients treated with topical metronidazole experienced significantly less postoperative pain compared to the placebo group throughout the 14- day observation period ($P \leq 0.04$). Notably, after-defecation pain in the metronidazole group was significantly lower on day 2 ($P = 0.016$), and patients required fewer additional analgesics on days 2 and 7 ($P \leq 0.04$). These findings suggest that the application of topical 10 percent metronidazole can be an effective strategy in reducing post hemorrhoidectomy discomfort and after-defecation pain when compared to a placebo control group.[8]

Xia et al., aimed to explore the impact of metronidazole, administered both orally and topically, on post-operative pain following excisional hemorrhoidectomy. The analysis included nine randomized controlled trials with a total of 523 patients. The primary outcome assessed was post-operative pain measured by the visual analogue score (VAS), while secondary outcomes included analgesia use, complications, and time to return to normal activity. The meta-analysis revealed that patients receiving metronidazole, regardless of the administration route (oral or topical), experienced significantly less post-operative pain compared to those in the comparison groups. The findings suggest that both oral and topical metronidazole effectively reduce post-operative pain, prompting the need for further research to determine the optimal route of administration.[9]

and patients here undertook surgery for grade 2, grade 3 and grade 4 haemorrhoids. The patients in this study were divided into three groups: one group, the control group; the second group received oral metronidazole post-operatively for 7 days; the third group received only topical metronidazole for 7 day. Findings in this study suggested less post operative pain the patients receiving metronidazole in topical form than in oral metronidazole and control group.[10]

Post-Defecation Pain-

There are 6 patients [14%] have post defecation pain in topical metronidazole group while 3 patients [6.8%] have found in oral metronidazole group. There's no significant difference in post-defecation pain between the two groups ($p = 0.31$). This suggests that regardless of the treatment group, participants experience similar levels of pain after defecation. This suggests that regardless of the treatment group, participants experience similar levels of pain after defecation.

Study done by **Ala et al.,** aimed to evaluate the efficacy of topical metronidazole (10 percent) in alleviating postoperative and after-defecation pain following hemorrhoidectomy in 47 patients. They found that patients treated with topical metronidazole experienced significantly less postoperative pain compared to the placebo group throughout the 14-day observation period ($P \leq 0.04$). These findings suggest that the application of topical 10 percent metronidazole can be an effective strategy in reducing post-hemorrhoidectomy discomfort and after-defecation pain when compared to a placebo control group.(8)

Duration to return to Normal Activity:

The mean return to normal activity after treatment with topical metronidazole was 9.066, with a standard deviation of 1.21. For oral metronidazole, the mean was 11.22, with a standard deviation of 1.3. there is a significant difference in the efficacy of topical metronidazole compared to oral metronidazole in facilitating the return to normal activity after treatment. Specifically, topical metronidazole appears to be more effective in this regard compared to oral administration.

The p-value associated with this comparison was 0.034, indicating a statistically significant difference in the return to normal activity between the two treatment groups. This suggests that there is a significant difference in the efficacy of topical metronidazole compared to oral metronidazole in facilitating the return to normal activity after treatment. Specifically, topical metronidazole appears to be more effective in this regard compared to oral administration.

A study done by **Xia et al.,** aimed to explore the impact of metronidazole, administered both orally and topically, on post-operative pain following excisional hemorrhoidectomy. The analysis included nine randomized controlled trials with a total of 523 patients. Both oral and topical metronidazole demonstrated a decrease in VAS means at all measured time points. There was no observed increase in complication rates, and patients receiving metronidazole returned to normal activity significantly earlier than the control groups. The findings suggest that both oral and topical metronidazole effectively reduce post-operative pain, prompting the need for further research to determine the optimal route of administration.[9]

Another similar study done by **Al-Mulhim et al.,** aimed to compare the impact of metronidazole on post-conventional hemorrhoidectomy pain in patients with third and fourth-degree hemorrhoids. Two hundred consecutive patients undergoing surgical treatment for 3rd and 4th degree hemorrhoids were randomly assigned to two groups. The metronidazole group demonstrated a significantly shorter return to normal activity. In conclusion, prophylactic metronidazole in Milligan-Morgan hemorrhoidectomy was associated with less pain and an earlier return to normal activity.[11]

5. Conclusion

This is a randomized control study, conducted in the department of General Surgery, Raipur institute of medical sciences, Raipur – Chhattisgarh, study will be conducted in year of 2022-2024 (18 months) after approval of institute's ethical committee. Main aim this study is ''To compare oral and topical metronidazole in early recovery of pain after open haemorrhoidectomy''.

The topical metronidazole group (D1) having 31.1% males, while the oral metronidazole group (D2) had a higher male composition of 38.8%. Topical metronidazole, frequencies ranged from 1 (81-90 years) to 12 (51-60 years) individuals, while for oral metronidazole, frequencies ranged from 0 (81-90 years) to 12 (51-60 years) individuals. Maximum patient ranged in age group between 40-60 years of age group in both groups. The topical metronidazole having 22% grade-2, 33% grade-3 and 44% grade-4 while the oral metronidazole had 2.2% grade-2, 56% grade-3 and 42% grade-4. Overall, 12% grade-2, 44% grade-3 and 43% grade -4 hemorrhoids patients found.

The mean VAS score between Group D1 (Topical Metronidazole) and Group D2 (oral metronidazole) which were all statistically significant when compared after 6 hours [p=0.04], after 12 hours [p=0.036], at day1 [p=0.01] and at day 3 [p=0.017]. We inferred that topical metronidazole showed a better pain control when compare to the oral metronidazole. The median baseline VAS score is 0.00 for both groups, indicating that participants in both groups reported no baseline pain on average. Participants in group D1 [topical metronidazole] consistently report lower pain levels compared to those in group D2 [oral metronidazole] across all time intervals.

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All being said, pain control in post hemorrhoidectomy patients is challenging. Studies and trials have been conducted with various with considerable number of drugs. Despite the advances in pain management in this modern era, pain management in these group of patients seems to be major challenge even in the hands of expert surgeons.

The conclusion of this study is as follows:

- Topical metronidazole has a favourable effect in pain control in the post hemorrhoidectomy patients in addition to antimicrobial effect as compared to oral metronidazole.
- Topical metronidazole as overall causes better patient satisfaction and earlier recovery and less post operative pain following open haemorrhoidectomy

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Master Chart

ID NO.	Age	Sex	Grade	Group Allocated	Visual Analogue Pain Scale					Post Defecation Pain	Return To Normal Activity
					0 Hour	6 Hour	12 Hour	24 Hour	72 Hour		
1	59	F	3	D1	1	6	5	3	2	NO	8
2	60	F	4	D2	2	9	8	7	6	NO	11
3	43	M	4	D1	0	6	4	4	2	NO	9
4	55	M	3	D1	0	3	4	4	3	NO	8
5	60	F	4	D1	1	4	4	2	2	NO	8
6	68	M	3	D2	2	8	6	4	4	YES	12
7	60	M	4	D2	2	8	7	7	6	YES	10
8	41	F	3	D2	2	8	7	7	7	NO	9
9	59	M	4	D1	0	4	4	4	4	NO	8
10	31	M	4	D2	1	9	7	7	5	NO	12
11	76	F	4	D2	1	8	8	6	6	NO	13
12	54	F	3	D2	1	9	9	9	7	NO	11
13	41	F	3	D1	2	4	3	3	2	NO	8
14	60	F	4	D1	0	5	4	3	3	YES	9
15	47	M	3	D2	0	9	9	8	7	NO	10
16	36	F	4	D1	0	4	4	3	2	NO	12
17	74	M	4	D2	0	8	8	8	7	NO	12
18	44	F	3	D2	1	8	7	7	7	NO	12
19	58	F	3	D2	2	9	9	8	8	NO	13
20	60	M	3	D1	2	4	3	3	2	YES	10

21	42	M	3	D2	3	9	8	6	6	NO	14
22	58	M	3	D1	1	3	3	2	3	YES	11
23	63	M	3	D2	3	8	9	8	7	NO	12
24	72	M	3	D1	0	6	4	4	4	YES	9
25	40	M	4	D1	0	4	3	2	2	NO	10
26	36	F	4	D1	0	4	2	2	1	NO	9
27	65	M	4	D2	1	6	7	7	6	NO	13
28	33	M	4	D1	1	4	3	3	2	NO	8
29	50	F	4	D2	2	8	8	7	6	NO	13
30	32	M	3	D1	1	4	2	3	3	NO	9
31	29	M	4	D2	1	8	8	6	6	NO	12
32	55	F	3	D1	0	3	2	2	3	NO	9
33	62	M	4	D2	0	8	8	7	7	YES	14
34	28	M	4	D1	1	5	4	4	4	NO	12
35	52	M	4	D2	0	7	8	7	7	NO	12
36	87	M	3	D1	0	6	4	4	3	NO	12
37	60	F	3	D1	0	6	3	2	2	NO	10
38	43	F	3	D2	1	7	7	7	6	NO	10
39	43	F	4	D1	0	3	3	3	3	NO	8
40	70	M	4	D2	2	9	9	8	8	NO	11
41	41	F	4	D1	1	3	2	3	2	NO	9
42	68	M	3	D1	0	3	4	3	3	NO	10
43	45	F	3	D1	0	4	2	4	3	NO	10
44	75	M	4	D2	0	8	8	7	8	NO	12
45	59	M	3	D1	0	4	4	4	4	NO	8
46	28	M	4	D2	0	9	8	8	7	NO	11