

Original Research Article

Is metronidazole a panacea for post-hemorrhoidectomy pain?

Probal Neogi, Anuvrat Sinha, Mayank Singh*

Department of Surgery, MLN Medical College and SRN Hospital, Allahabad, Uttar Pradesh, India

Received: 19 August 2018

Accepted: 27 September 2018

***Correspondence:**

Dr. Mayank Singh,

E-mail: dr.mayanksingh78@gmail.com

Copyright: © the author(s), publisher and licensee Medip Academy. This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License, which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

ABSTRACT

Background: Pain following Milligan Morgan hemorrhoidectomy is a significant cause of morbidity. The present study was carried out to find out if using metronidazole in the post-operative period of these patients results in less post-operative pain.

Methods: This was a prospective randomized controlled trial which was conducted on 67 consecutive patients attending the Surgical OPD at SRN Hospital, Allahabad during the study period between August 2016 and July 2017 who underwent surgery for grade 2, grade 3 and grade 4 hemorrhoids. The patients were allocated to 3 groups-one group was the control group, the second group received oral metronidazole post-operatively for 7 days while the third group received only topical metronidazole for 7 days. All the three groups received 500 mg of metronidazole in 100 ml infusion pre-operatively. The post-operative analgesic usage was standardized for all the three groups. Appropriate tests of significance were applied to assess if the difference in the intensity of post-operative pain was significant in the immediate post-operative period and on days 1, 3 and 7 post-surgery.

Results: Pain relief was significantly better in the groups using metronidazole at post-operative day 1, 3 and 7 and this was also borne in the lesser number of analgesics used by the patients of these groups.

Conclusions: Use of oral or topical metronidazole in the post-operative period results in clinically significant pain relief. There is no additional benefit of one over the other and hence either can be used.

Keywords: Hemorrhoidectomy, Haemorrhoids, Pain, Metronidazole, VAS

INTRODUCTION

Today hemorrhoids remain the most common anorectal disorder and are frequently seen in primary care clinics, emergency wards, gastroenterology units and surgical clinics.¹ These patients may present with rectal discomfort, swelling, pain, discharge, and bleeding at the time of defecation and a full evaluation of these complaints is necessary, in the form of a detailed history and clinical examination which includes (but not limited to) digital rectal examination and rigid proctoscopy.

Indications for surgery include failure of non-operative management, acute complicated hemorrhoids such as

strangulation or thrombosis, patient preference and concomitant anorectal conditions such as anal fissure or fistula in ano. Common surgical methods used in contemporary practice today are Open (Milligan-Morgan) Hemorrhoidectomy, Closed (Ferguson) Hemorrhoidectomy and Stapled Hemorrhoidopexy.³

The major post-operative complications of hemorrhoidectomy are pain, infection, hemorrhage, urinary retention, anal stenosis, fecal incontinence and non-healing wound.⁴ Postoperative pain after a Milligan-Morgan hemorrhoidectomy, which is still the most commonly performed surgery today, remains a major problem for anorectal surgeries all over the world.

The spasm of internal anal sphincter appears to be the main culprit for causing post hemorrhoidectomy pain while the other reason being secondary infection in the wound due to bacterial colonization.⁵ Various invasive and non-invasive methods have been suggested to relieve internal sphincter spasm and hence alleviate post-hemorrhoidectomy pain. These include Glyceryl Trinitrate cream, calcium channel blockers, Botox Injection, Bupivacaine and Metronidazole.⁶ This study investigated whether the use of metronidazole resulted in clinically significant reduction in pain in post-operative period.

METHODS

All patients aged 20 years and above with Grade 2, 3 or 4 hemorrhoids attending the surgical OPD at SRN Hospital, Allahabad from August 2016 to July 2017, who were willing for open surgery and were able to comprehend and consent, were included in the study. Patients of early Grade I hemorrhoids or with co-existing anal pathologies or with serious life-threatening illnesses (ASA status III, IV, V) or allergies to Metronidazole were excluded. The patients thus included, were assessed by a detailed history and clinical examination including digital rectal examination and rigid proctoscopic examination. Routine baseline investigations were done and fitness for surgery assessed followed by randomization into treatment groups.

The Block Randomization technique was used to allocate the patients into three groups: G1 (control), G2 (post-operatively oral metronidazole for 7 days) and G3 (topical metronidazole for 7 days). 21 patients were allocated to G1, 23 to G2 and 23 to G3. 7 patients were lost to follow up and after removing them, 20 patients remained in each of these groups, making a total of 60. Pre-operative antibiotic (in the form of injectable metronidazole) and post-operative analgesic usage were standardized for all the three groups.

The Visual analogue scale (VAS) for pain, a widely used unidimensional measure of pain intensity, was used to assess the patients immediately post-operatively and at day 1, 3 and 7 post surgery. The day of surgery was taken as day zero.

Based on the distribution of pain, VAS scores in post-operative patients were described as no pain (0-1), mild (2-4), moderate (5-7) and severe (8-10). After removing the patients who were lost to follow-up, ANOVA and post-hoc Games-Howell tests were applied to test for clinical significance within the different groups.

RESULTS

Out of the net 60 patients that remained (after excluding those who were lost to follow-up), with 20 patients in each of the 3 groups, Group 1 (G1) became the control group, Group 2 (G2) was given only oral metronidazole tablets and Group 3(G3) received only topical metronidazole.

Although the study was open to female subjects as well, none of them turned up for surgical intervention. Hence all the patients in our study were males. A good majority (46.6%) of patients in each treatment regimen were in the age group between 35 to 45 years; 10 in Group 1, 11 in Group 2, 7 in Group 3.

32 patients (53.3%) had a history of shorter duration (less than 5 years) and 28 (46.6%) had it for a longer time (5 years or more). Out of the 60 patients, 10 (16.6%) had Grade 2 hemorrhoids, 20 (33.3%) had Grade 3 hemorrhoids and 30 (50%) had Grade 4 hemorrhoids. As far as the complications of hemorrhoids were concerned, 9 (15%) patients had thrombosed hemorrhoids, 4 (6.6%) patients were anemic and 47 (81.6%) were free from these complications.

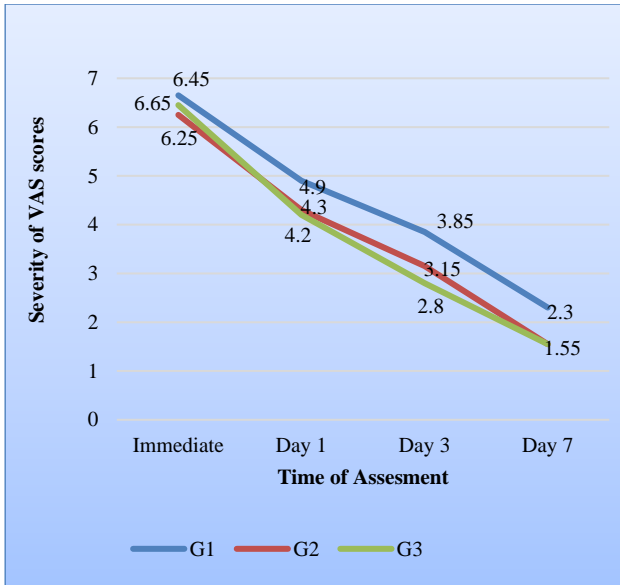
Table 1: Comparison of VAS scores of different regimens in the post-operative period.

Duration	G1 (Mean±SD)	G2 (Mean±SD)	G3 (Mean±SD)	p-value (of ANOVA)*
Immediate Post-operatively	6.65±0.74	6.25±0.78	6.45±0.88	0.30161 (not significant)
D1	4.90±0.71	4.30±0.65	4.20±0.76	0.00604 (significant)
D3	3.85±0.74	3.15±0.81	2.80±0.76	0.00000 (significant)
D7	2.30±0.57	1.55±0.68	1.55±0.51	0.00011 (significant)

*Results were significant only if p-value <0.05

In the immediate post-operative period for the first group, the mean value of VAS was 6.65±0.74; for the second, it was 6.25±0.78; for the third group, it was 6.45±0.88. After applying one-way ANOVA test on VAS values for G1, G2 and G3 in the immediate post-operative period, the result was not significant at p <0.05.

Thus, metronidazole by any route of administration was not an effective analgesic, in the immediate post-operative period. However, on post-operative day 1, the result was significant (p<0.05). VAS scores were 4.9±0.71 for the control group; 4.3±0.65 and 4.2±0.76 for G2 and G3 respectively.



G1: Control Group; G2: Oral Metronidazole Group; G3: Topical Metronidazole Group

Figure 1: Comparative VAS pain scale scores of the three groups.

The result was similar to Day 1 for post-op Day 3 and Day 7. Their results were significant for pain relief during this period. The VAS scores were 3.85 ± 0.74 , 3.15 ± 0.81 and 2.80 ± 0.76 for the groups G1(Control), G2 and G3 respectively on Day 3 and 2.30 ± 0.57 , 1.55 ± 0.68 and 1.55 ± 0.51 for the groups G1(Control), G2 and G3 respectively on Day 7.

Figure 1 shows a line diagram depicting the trend of severity of pain at different points of time post-operatively in the three treatment groups.

Table 2: Significance of difference in vas pain scores in the three regimens (at p-value <0.05) using Games-Howell test.

DURATION	G1 vs G2	G1 vs G3	G2 vs G3
Immediate post-op (1/2 hour after surgery)	Not significant	Not significant	Not significant
Day 1	Significant	Significant	Not significant
Day 3	Significant	Significant	Not significant
Day 7	Significant	Significant	Not significant

Another significant observation as apparent from Table 2 is that there was no additional benefit of topical over oral metronidazole, using the Games-Howell Test. Also, there was a statistically significant difference (after applying one way-ANOVA test, p value was less than 0.05) among the three groups with regard to the number of extra

analgesic tablets and the number of days for which they were taken as evident from Table 3.

Table 3: Comparison of the number of extra analgesic tablets used and number of days of extra analgesic with each regimen.

Regimens	No. of extra tablets used (Mean±SD)	No. of days (Mean±SD)
G1	8.95 ± 5.11	4.00 ± 1.65
G2	3.85 ± 3.57	1.65 ± 1.22
G3	2.20 ± 2.01	1.00 ± 0.85

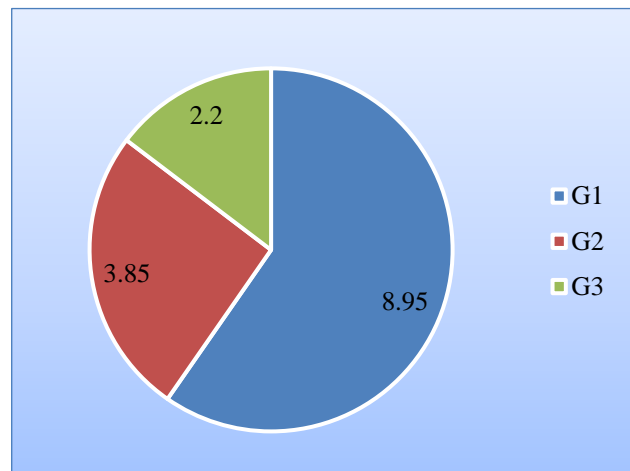


Figure 2: Mean number of extra analgesic tablets.

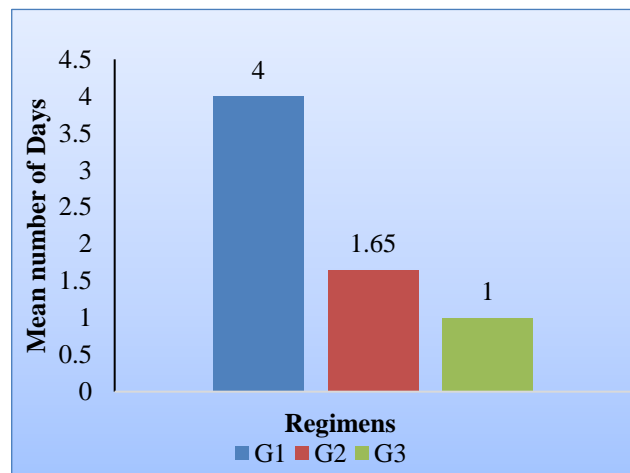


Figure 3: the mean number of extra days that the patients of the three groups took analgesic tablets.

Figure 2 and the Figure 3 are the graphical representations depicting the number of extra tablets and the extra number of days respectively for which analgesic tablets were post-operatively used in the three groups. Maximum analgesic requirement was found to be in the control group (G1) and minimum was in the topical metronidazole group(G3).

DISCUSSION

In the present study, it was found out that in the immediate post-operative period, i.e. when assessed at half an hour after surgery, the difference in the VAS scores of the patients was not significant but it was significant on post-operative day 1, 3 and 7. In a study by Carapeti et al (1998), patients who were on oral metronidazole for 7 days after surgery had significantly less pain than the control on days five, six and seven. Patient satisfaction was also better with the procedure in the metronidazole group.⁷ Holzheimer et al used topical 10 percent metronidazole which was applied to the surgical site and patients had significantly less postoperative pain than those in the placebo group by day 14.⁸ The study by Ala S et al also indicates that topical 10 percent metronidazole significantly reduce post hemorrhoidectomy discomfort and also pain during defecation postoperatively compared with that of the placebo control group.⁹

Similar results were obtained in the studies conducted by Lopez et al where the post-operative pain differed significantly between the study group (metronidazole group) and the control group (placebo group) post-operatively at 6 h, 12 h, 24 h, day 4, 7 and day 14. Also, the analgesic consumption was needed for a shorter duration in the oral metronidazole group as compared to the control group.¹⁰ The exact mechanism of Metronidazole causing pain relief is not known. Speculations of relief of anal sphincter spasm and prevention of secondary infection have been proposed. But a significant finding of our study was the fact that there was no difference in using metronidazole in either the topical or oral form. This probably, would refute the logic of local effect of metronidazole acting as an antispasmodic to relieve post hemorrhoidectomy pain.

CONCLUSION

Continuation of metronidazole in the form of oral or topical preparation in the post-operative period results in better pain relief and less use of analgesic drugs and therefore could correlate to earlier return to daily life activities as compared to its administration as pre-operative antibiotic only. There is no additional benefit of topical metronidazole over oral metronidazole in pain relief in the post-operative period after surgery and hence both can be used interchangeably.

ACKNOWLEDGEMENTS

Authors acknowledge the help of faculty in the Department of Surgery who helped in the collection of

adequate sample size of the patients. Authors also like to acknowledge the contribution of faculty of Department of Preventive Medicine who helped in carrying out the statistical analysis of the data.

Funding: No funding sources

Conflict of interest: None declared

Ethical approval: The study was approved by the Institutional Ethics Committee

REFERENCES

1. Welling DR, Wolff BG, Dozois R. Piles of defeat: Napoleon at Waterloo. *Dis Colon Rectum*. 1988;31(4):303-5.
2. Milligan ET, Morgan CN, Jones LE, Officer R. Surgical anatomy of the anal canal and operative treatment of haemorrhoids. *Lancet*. 1937;11:1119-94.
3. Pescatori M. Closed hemorrhoidectomy. *Ann Ital Chir*. 1995;66:787-90.
4. Joshi GP, Jaschinski T, Bonnet F, Kehlet H. Prospect collaboration. *BMC Anesthesiol*. 2015;15:159.
5. Al-Mulhim AS, Ali AM, Al-Masoul N, Alwahidi A. Post hemorrhoidectomy pain: a randomized controlled trial. *Saudi Med J*. 2006;27(10):1538-41.
6. Rohimi R, Abdollahi M. A systematic review of the topical drugs for post hemorrhoidectomy pain. *IJP*. 2012;8(7):628-37.
7. Carapeti EA, Kamm MA. Double blind randomised controlled trial of the effect of metronidazole on pain after day care hemorrhoidectomy. *Lancet*. 1998;351(9097):169-72.
8. Holzheimer RG. Hemorrhoidectomy-indications and risks. *Eur J Med Res*. 2004;9(1):18-36.
9. Ala S, Saedi M, Eshghi F, Mirzabeygi P. Topical metronidazole can reduce pain after surgery and pain on defecation in postoperative hemorrhoidectomy. *Dis Colon Rectum*. 2008;51(2):235-8.
10. Solorio-López S, Palomares-Chacón UR, Guerrero-Tarín JE, González-Ojeda A, Cortés-Lares JA, Rendón-Félix J, et al. Efficacy of metronidazole versus placebo in pain control after hemorrhoidectomy. Results of a controlled clinical trial. *Rev Esp Enferm Dig*. 2015;107:681-5.

Cite this article as: Neogi P, Sinha A, Singh M. Is metronidazole a panacea for post-hemorrhoidectomy pain? *Int Surg J* 2018;5:3598-601.