

## Original Research Article

# A study of analgesic effect of methylene blue injection in post conventional haemorrhoidectomy

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### ABSTRACT

**Background:** Haemorrhoids are common perianal disease. Milligan-Morgan haemorrhoidectomy operation is a classical haemorrhoid resection procedure that has been widely used as gold standard. Classical haemorrhoidectomy is associated with considerable postoperative pain. This leads to patient discomfort; prolonged hospital stays and increased cost. The causes of post haemorrhoidectomy pain are multifactorial. Methylene blue has been widely used as biological dye. It is an inhibitor of soluble guanylate cyclase. It has also been found to reduce cyclooxygenase products. The mechanism of action of methylene blue is likely to be related to the destruction of dermal nerve endings.

**Methods:** A prospective study of 114 indoor patients was conducted to compare the effects of 1% intradermal methylene blue injection at local site and injection paracetamol (I.V.) as per requirement after Milligan-Morgan haemorrhoidectomy admitted to Surat municipal institute of medical education and research (SMIMER) hospital at Department of General Surgery. Samples were divided into two groups each of 57 patients, in case group patients were given intradermal methylene blue at local site after haemorrhoidectomy and in both groups' injection paracetamol was given as per requirement. Both groups are assessed by visual analogue scale (VAS).

**Results:** Present study concluded that mean post-operative score according visual analogue scale (VAS) in case group was significantly lower as compared to control group on 1st and 3rd post-operative day.

**Conclusions:** Methylene blue injection has an analgesic effect at local site after post conventional haemorrhoidectomy without any significant side effects of methylene blue.

**Keywords:** Methylene Blue, Milligan-Morgan haemorrhoidectomy, Open haemorrhoidectomy, Post-operative pain

### INTRODUCTION

Haemorrhoids are considered one of the most common anorectal diseases with a prevalence of 4.4% up to 36.4% of the general population, and a peak incidence between 45 and 65 years.<sup>1,2</sup>

Haemorrhoids are clusters of vascular tissue, smooth muscle, and connective tissue arranged in 3 columns along the anal canal. They are present in healthy individuals as cushions that help to maintain continence.

Although haemorrhoids are normal structure, the term haemorrhoid has come to refer to a pathologic or symptomatic process.<sup>3</sup>

Haemorrhoidal disease presents with a prolapsed lump, painless bleeding, discomfort, discharge, hygiene problems, soiling, and pruritus.<sup>4</sup> Sliding anal canal lining theory is the most accepted theory as a cause of haemorrhoidal disease; however, it is also associated with hyper-vascularity, and, recently, with several enzymes or mediators involved in the disintegration of the tissues

supporting the anal cushions, such as matrix metalloproteinase.<sup>5</sup>

Treatment modalities includes conservative treatment (life style modification, oral medications, and topical treatment), office procedures (rubber band ligation, injection sclerotherapy, infrared and radiofrequency coagulation, bipolar diathermy and direct-current electrotherapy, cryosurgery, and laser therapy), as well as surgical procedures including diathermy haemorrhoidectomy, LigaSure haemorrhoidectomy, Harmonic scalpel haemorrhoidectomy, haemorrhoidal artery ligation, stapled haemorrhoidopexy (SH), and suture haemorrhoidopexy. Surgical procedures are effective at eliminating haemorrhoids but may be painful.<sup>6</sup>

Pain after haemorrhoid surgery remains one of the most important patient complaints.<sup>7</sup>

Excision haemorrhoidectomy is most commonly used for 3<sup>rd</sup> and 4<sup>th</sup> degree haemorrhoids. After haemorrhoid surgery, pain is reported in the early postoperative period but also after 2-3 days, around the time of first defecation.

Perianal injection of methylene blue has shown to ablate perianal nerve endings and relieve pain relief after haemorrhoidectomy.

Our present study shows that methylene blue injection has an analgesic effect in post conventional haemorrhoidectomy

## **METHODS**

A prospective randomized study was conducted among indoor patients admitted to Surat Municipal Institute of Medical Education and Research (SMIMER) hospital at Department of General surgery.

The study was conducted over a period of 18 months from February 2020 to August 2021. It was a prospective study. The patient selection was by done by simple random sampling.

During this study period 114 patients were admitted with haemorrhoids.

### ***Inclusion criteria***

Patient having symptomatic haemorrhoids. Patient willing to give consent for the study. Patient between 21 to 60 years undergoing conventional haemorrhoidectomy.

### ***Exclusion criteria***

Lactating women. Patients who experienced any ill-effects from previous methylene blue use. Patients who

were undergoing combined procedures for fissures or fistulae.

## ***Methodology***

The whole sample was divided into randomly two equal and comparable groups of each 57 patients- Case and control.

in case group, after the haemorrhoids are excised, methylene blue 1% is injected intradermal approximately 1 cm away from incision edge. The needle orientation was approximately 45° from skin. Uniform injections were given at each injection point in the upper, lower, left, and right direction with 1ml of injection drug per injection point. The distance between every two injection points is 1 cm. After injection, the drug is spread evenly by gentle rubbing the area with gauze. Injection paracetamol (150 mg/2 ml) is given as per requirement.

In control group, after haemorrhoids are excised, injection paracetamol (150 mg/dl) is given as per requirement. Both groups are assessed by visual analogue scale (VAS).

## ***Statistical analysis***

All statistical analysis was performed using SPSS 25 (Statistical Package for Social Science). Quantitative variables were presented as means or as median (range).

## ***Ethical approval***

The study was approved by the Institutional Ethics Committee.

## **RESULTS**

Present study was conducted among 114 cases (case group: 57, control group: 57) diagnosed with haemorrhoids and undergoing for conventional haemorrhoidectomy with aim to study the analgesic effect of methylene blue injection at local site in post conventional haemorrhoidectomy.

Highest numbers of participants were noted in 51-65 years age group in both the study groups (38.6% & 36.8%). Mean age was also similar in both the groups but it was not statistically significant ( $p>0.05$ ) (Table 1). Male: female ratio was 1:0.8 and 1:0.4 in case and control group respectively ( $p>0.05$ ) (Table 2). Bleeding PR and pain were the most common symptoms observed among study participants (Table 3).

Most of the patient (94.7% and 96.5%) of both the groups were presented with grade 3 piles ( $p>0.05$ ) and almost 3/5th cases (63.2% and 68.4%) of both the groups have internal piles. Mean duration of surgery was statistically non-significantly almost similar in both the groups

( $p > 0.05$ ). Mean duration of hospital stay was statistically significantly almost similar in both the groups ( $p < 0.05$ ).

Mean post-operative score was statistically significantly lower in case group compare to control group at 1st and 3rd day of post-operative ( $p < 0.05$ ). Mean post-operative score was statistically non-significantly lower in case group compare to control group at 5th, 15th and 28th day of post-operative ( $p > 0.05$ ) (Table 4). Post-operative complications were higher in number in control group compare to case group (Table 5). 'Wound healing after 1

month' noted in all participants of case group and more than 95% participants of control group (Table 6).

All participants of control group and only almost 1/4th (26.3%) of case group required post-operative PCM injection which indicated that post-operative analgesic injection required statistically significantly very less in number in case group compare to control group ( $p < 0.05$ ) (Table 7). 'Number of haemorrhoids Excised' was statistically non-significantly almost similar in both the groups ( $p < 0.05$ ).

**Table 1: Age distribution of study participants (n=114).**

Age group	Group (n=114)		Group (n=114)		p value
	Case (n=57)	%	Control (n=57)	%	
21-35	15	26.3	16	28.1	0.54
36-50	20	35.1	18	31.6	
51-65	22	38.6	21	36.8	
>65	0	0.0	2	3.5	
Mean ±SD	43.1±9.7		42.7±11.8		0.67

**Table 2: Gender distribution of study participants (n=114).**

Gender	Group (n=114)		Group (n=114)		P value
	Case (n=57)	%	Control (n=57)	%	
Male	31	54.4	40	70.2	0.12
Female	26	45.6	17	29.8	

**Table 3: Most common symptoms noted among study participants (n=114).**

Symptoms	Group (n=114)		Group (n=114)		P value
	Case (n=57)	%	Control (n=57)	%	
Bleeding PR	37	64.9	33	57.9	0.56
Pain	20	35.1	24	42.1	

**Table 4: Mean post-operative pain score (n=114).**

Post-operative interval (in day)	Group (n=114) (mean±SD)		P value
	Case (n=57)	Control (n=57)	
1 <sup>st</sup>	3.7±2.1	5.3±3.4	0.01
3 <sup>rd</sup>	3.5±2.5	4.6±2.8	0.02
5 <sup>th</sup>	2.8±2.4	3.1±2.0	0.45
15 <sup>th</sup>	2.4±2.4	2.5±1.8	0.32
28 <sup>th</sup>	1.9±2.2	1.9±1.3	0.07

**Table 5: Post-operative complication distribution of study participants (n=114).**

Complication	Group (n=114)	
	Case (n=57)	Control (n=57)
Pain requiring readmission	0	2
Acute urinary retention	2	4
Secondary hemorrhage	0	3
Pruritus	1	0
Local skin reaction	0	1
Temporary incontinence	1	1

**Table 6: Distribution of study participants according to wound healing after 1 month (n=114).**

Wound healing after 1 month	Group (n=114)				P value
	Case (n=57)	%	Control (n=57)	%	
Yes	57	100.0	55	96.5	0.48
No	0	0.0	2	3.5	

**Table 7: Comparison of 'number of additional analgesic (Inj. Paracetamol) taken' among study participants (n=114).**

Post-operative injection PCM required	Group				P value
	Case (n=57)	%	Control (n=57)	%	
Yes	15	26.3	57	100	<0.001
No	42	73.7	0	0	

## DISCUSSION

Present study was conducted among 114 cases (case group: 57, control group: 57) diagnosed with haemorrhoids and undergoing for conventional haemorrhoidectomy surgery at Department of Surgery, SMIMER Medical College Surat.

The highest numbers of participants were noted in 51-65 years age group in both the study groups (38.6% and 36.8%). Mean age was also similar in both the groups but it was not statistically significant. A similar result has been observed in our reference studies Sim et al and Xiang et al.<sup>8,9</sup>

The male: female ratio was 1:0.8 and 1:0.4 in case and control group respectively ( $p>0.05$ ) which was similar to studies like Sim et al and Xiang et al.<sup>8,9</sup>

Methylene blue, also known as methylthioninium chloride, is a salt used as a medication and dye. It was used in treatment of malaria, cyanide poisoning and urinary tract infection. Mainly now it is used in treatment of methemoglobinemia, when methemoglobin levels that are greater than 30% or in which there are symptoms despite oxygen therapy. In surgeries such as sentinel lymph node dissections, methylene blue can be used to visually trace the lymphatic drainage of tested tissues.<sup>10</sup> Similarly, methylene blue is added to bone cement in orthopedic operations to provide easy discrimination between native bone and cement.

Additionally, methylene blue accelerates the hardening of bone cement, increasing the speed at which bone cement can be effectively applied. However, methylene blue has been rarely used in analgesia. In recent years, local injection of methylene blue has been evaluated in treatments for various pain diseases and has shown a remarkable long-acting analgesic effect.<sup>11</sup>

There are various methods available in treatment of haemorrhoids but classical haemorrhoidectomy remains one of the most commonly performed method as it is cost

effective compared to other methods like stapled haemorrhoidopexy and Doppler Haemorrhoidal artery ligation. But most common symptom remains post-operative pain after haemorrhoidectomy.<sup>12</sup>

Methylene blue is a nontoxic dye agent that inhibits the soluble guanylate cyclase and nitric oxide synthase.<sup>13</sup> Nitric oxide regulates physiological functions such as pain and analgesia by activating soluble guanylate cyclase to increase intracellular cyclic guanosine monophosphate. Methylene blue, as an oxidizing-reducing agent, demonstrates a strong affinity to nerve tissues when applied locally, which can directly block the electrical conductivity of nerve fibres, thereby affecting the neural excitability and impulse conductivity. Recent studies have shown that a low dose (0.5% or 1%) of methylene blue may block peripheral nerve fibres at the incision. A local injection of methylene blue could cause reversible damage to the incision and its surrounding subcutaneous nerve terminal medulla, thus achieving a long-acting postoperative analgesic effect.

In present era, there are various analgesics to control post-operative pain. In our study there is significant reduction in post-operative pain scores in case group after giving local injection of methylene blue after conventional haemorrhoidectomy in first three days. The result of our study showed that case group has significant reduction in VAS score in 1st and 3rd day after surgery as compared to control group. Mean post-operative score was statistically non-significantly lower in case group compare to control group at 5th, 15th and 28th day of post-operative ( $p>0.05$ ). This suggests that local injection of perianal methylene blue has a significant analgesic effect after conventional haemorrhoidectomy. A similar result has been observed in our reference studies Sim et al and Xiang et al.<sup>8,9</sup>

There were no significant side effects of methylene blue injection. Also wound healing after 1 month was similar in both groups. The use of postoperative injection Paracetamol was comparatively higher in control group as compared to case group.<sup>14</sup> This suggests that the

requirement of analgesia was comparatively lower in case group as compared to control group.

### Limitations of study

For more acceptable results, it is advisable to perform the study by recruiting higher number of cases.

### CONCLUSION

From the present study we would like to conclude that mean post-operative score according visual analogue scale (VAS) in case group was significantly lower as compared to control group on 1<sup>st</sup> and 3<sup>rd</sup> post-operative day. So, it is concluded that injection methylene blue has an analgesic effect at local site after post conventional haemorrhoidectomy without any significant side effects of methylene blue.

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