

Low Dose Intrathecal Morphine versus Multimodal Analgesia in Patients Undergoing Abdominal Surgeries under General Anaesthesia

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Abstract

Original Research Article

Introduction: Opium means juice, from Greek word. Morphine is named after Greek god of dreams, Morpheus Opioid refers to drugs derived from opium both natural and synthetics. Narcotic refers to morphine and like analgesics. **Aim of the Study:** To evaluate the effect of preservative free morphine 0.5mg administered intrathecally, on intraoperative anesthetic requirement and post operative analgesia in patients undergoing laparotomies under general anesthesia compared with multimodal analgesia during the 1st 24 hours of postoperative period. **Materials And Methods:** This study was conducted at Sheikh Sayera Khatun Medical College & Hospital, Gopalganj, Bangladesh during from Jun to December 2019, in the general surgical operation theater. 50 patients of ASA physical status I, II and III undergoing both upper and lower abdominal surgeries under general anesthesia are categorized into one of two groups, Group M – Morphine study group and Group C – Control group. In both study and control Group routine General anesthesia was administered. In Group M, 0.5mg morphine given intrathecally before general anaesthesia. The parameters studied were intraoperative hemodynamics, post operative pain score and analgesic requirement, post-operative hemodynamics, intra operative and post-operative complications. **Results:** The number of demand analgesia in 24 hours is 1.56 in Group – M vs 4.2 in Group- C and it is statistically significant ($p=0.0002$). Post operative visual analog score (VAS) in Group-M was 4.64 vs 5 in group – C. But it was highly significant at 2,4,8,12,20 hours and . However, it was not significant at postoperative zero hours, 14, 16,24 hours. Postoperative Ramsay sedation scale (RSS) is 2.16 in group – M, 1.6 in Group – C, this is statistically significant ($P=0.0156$). The postoperative heart rate in group –M vs Group – C are 85 ± 12.7 and 101 ± 13.9 respectively and it statistically significant ($p=0.0002$). The post operative mean arterial pressure (MAP) is 89 ± 15.7 group- M vs 104 ± 14.3 Group - C which is statically significant ($P=0.0012$). **Conclusion:** Intrathecal morphine produced better postoperative analgesia and sedation. Intrathecal morphine group demonstrated lesser amounts of analgesic and rescue analgesic requirement during the postoperative period. Intrathecal morphine produced better hemodynamic stability in the postoperative period. Intrathecal morphine produced side effects in the form of nausea, vomiting, hypotension and bradycardia but not statistically significant.

Keywords: General anesthesia, abdominal surgeries hemodynamics, post-operative complications.**Copyright @ 2020:** This is an open-access article distributed under the terms of the Creative Commons Attribution license which permits unrestricted use, distribution, and reproduction in any medium for non-commercial use (NonCommercial, or CC-BY-NC) provided the original author and source are credited.

INTRODUCTION

Opium means juice, from Greek word. Morphine is named after Greek god of dreams, Morpheus Opioid refers to drugs derived from opium both natural and synthetics. Narcotic refers to morphine and like analgesics. Morphine can be used as spinal analgesic, epidural analgesic [1]. Despite the high efficacy, it was not widely used because of high incidence of respiratory depression and somnolence, It was due to high doses, rather than route of administration. Gwartz and associates reported high patient satisfaction and low incidence of side effects

and complication of morphine over 6000 patients [2]. Therefore, this study has been undertaken to analyze the effect of intrathecal morphine as more cost effective analgesic when compare to multimodal analgesia. Long-acting opioids are considered the cornerstone of single-injection IA for postoperative pain. While morphine has been considered the gold standard opioid for IA, recent national drug shortages have limited its availability. Hydromorphone is an alternative long-acting opioid that has grown in popularity, particularly for chronic pain. Its role in acute postoperative pain is less clear. Limited data exist on the safety, efficacy, and optimal IA medication regimen in the setting of an ERP

including open and laparoscopic surgery. Therefore, we aimed to describe the efficacy and safety of IA, including intrathecal hydromorphone, in a cohort of colon and rectal surgical patients in a standardized ERP program. Enhanced recovery pathways have been shown to decrease morbidity, length of hospital stay, and costs in colorectal surgery [16, 17]. These pathways are designed to accelerate patient recovery and focus on certain key components—early feeding, maintenance of euolemia, optimization of pain control (with limitation of systemic opioids), and early ambulation [17-19]. Multimodal analgesia is an essential component of an enhanced recovery pathway (ERP). The use of continuous, low-thoracic epidural analgesia has long been cited as a beneficial and effective mode of analgesia in colorectal surgery [20].

AIM OF STUDY

To evaluate the effect of preservative free morphine 0.5mg administered intrathecally, on

intraoperative anesthetic requirement and post operative analgesia in patients undergoing laparotomies under general anesthesia compared with multimodal analgesia during the 1st 24 hours of postoperative period.

MATERIALS AND METHODS

This study was conducted at Sheikh Sayera Khatun Medical College & Hospital, Gopalganj, Bangladesh during from Jun to December 2019, in the general surgical operation theater.

- The study was done after getting Institutional Ethical Committee approval
- Written informed consent were obtained from all patients included in the study

All patients were explained about the procedure and visual analog scale (Pain score) 10cm scale so that it can be effectively used by the patient during the post-operative period.

Inclusion criteria	Exclusive Criteria
A.SA I,II,III patients	patient refusal
Those patients who are undergoing upper and lower abdominal surgeries	Contraindication to subarachnoid block
	Hypersensitivity to study group
	Difficult airway MMS**>3
	5. Hepatic and renal dysfunction

50 patients of ASA physical status I,II and III undergoing both upper and lower abdominal surgeries like partial Gastrectomy ,open cholecystectomy, incisional hernia, Hemicolectomy and laparotomy under general anesthesia. The patients are categorized into one of two groups.

- Group M–Morphine – study group
- Group C– Control group

All patients were assessed preoperatively using standard protocols and underwent preoperative evolution. All patients were premeditated with T.alprazolam, T. Ranitidine 150mg P. O. the night before surgery and on the day of surgery 2hours before operation P.O, with sips of water. Preservative free morphine sulphate 10mg/ml is diluted to 10ml with sterile normal saline. In study Group M patients were hooked on monitors E.C.G, Pulse oximetry and Non invasive BP. Two IV access with 18G IV cannula was obtained .500ml of normal saline was preloaded. Patients was turned right lateral position .Patient back was painted with antiseptic solution and draped. Morphine was taken in 0.5 mg diluted to 1 cc with normal saline .Subarachnoid block was done with 25G Quinckie spinal needle at L3-L4 ISS after confirming free flow of CSF ,1ml of preservative free morphine

0.5mg was administered intrathecally and patient turned supine position and observed for 10min before induction of GA. Preoxygenation done for 3mins. In both study and control Group Routine General anesthesia was administer with Inj. Glycopyrrolate 0.2mg +Fentanyl 2µg/kg i.v., and Induction with Inj.Thiopentone 5mg /kg + suxamethonium 2mg/kg after 60 seconds patient incubated with 8 or 8.5 mm cuffed ETT orally for male,7 or 7.5 mm orally in female patients .All patients were catheterized to monitor urine output. Relaxant Inj.Vecuronium 0.12 mg/kg given IV. Maintains with oxygen 50% with Nitrous oxide with volatile agent isoflurane 1%. IV fluids were given according to body loss and 3rd space loss .Vitals were recorded every 5minutes until the end of surgery PR, BP, SPo2.Injection Diclofenac sodium 75mg IV infusion was started after one hour of surgery in both groups .Fentanyl 20µg IV top up per hour. At the End of surgery after replacing blood losses and fluids patient was reversed with Inj. Neostigmine 0.05 mg/kg+Glycopyrrolate 10µg/kg. After through suctioning and good attempts patient was extubated on table if hemodynamically stable. Patient was shifted to Surgical ICU and monitored by concerned anesthesia PG .All patients were given oxygen by venti mask 4 liter /min and 30° Head up was given.

Pain assessed by visual analog scale (VAS).every hour until 4th hour and thereafter every 2nd hours for 24 hours.

Group	Group M – Morphine	Control Group
If VAS >4	Inj. Diclofenac 75mg im	Inj.Diclofenac 75mg Im b.d and inj.Tramadol 100 mg i.v. t.d.s
rescue analgesic	inj.Fentanyl 20 µg titrated to response	inj.Fentanyl 20 µg titrated to response

Recovery characteristics include VAS score, Ramsay sedation scale, postoperative HR, BP, saturation, complication and effects of opioids were monitored and noted. The other parameters monitored in the post operative period included

1. Time for 1st demand analgesia,
2. No. of Analgesia doses in 1st 24hours
3. No of NSAID doses in 1st 24 hours
4. No of Rescue analgesic doses in 24 hours, The Complication monitored included
 - Retention of urine
 - Respiratory depression .It is defined as a respiratory rate < 8 / min and or oxygen saturation<90 %.This was planned to be managed with bag and mask ventilation or intubation and I.P.P.V. if necessary naloxone 0.2 mg IV every 5-10 mins till normal breathing pattern was established
 - Nausea and vomiting managed with Inj.ondansetron 8 mg intravenously
 - Pruritis
 - Hypotension
 - Bradycardia

Ramsay Sedation score (RSS). It has six scores

1. Anxious and agitated or restless or both.
2. Cooperative oriented and tranquil
3. Responds to commands only
4. Asleep with brisk response to light glabellar tap or loud auditory stimulus.
5. Asleep with sluggish response to stimulus.
6. Asleep with no response to Stimulus.

A sedation score greater than 4th was considered significant and observed for 24th hours and

then shifted to post operative ward .The patient study was completed after 24 hours of intrathecal morphine.

Study Sample and Data Analysis

A total of 50 cases each were randomly allocated to one of the following two groups via Group – M (Morphine) and Group–C (Control).The Information collected all the cases were recorded in a Master Chart. Data analysis was done with the help computer using Epidemiological Information Package (EPI 2002). Using this software, frequencies, Percentages, means, Standard deviation, Chi square and ‘p’ values were calculated.’p’ values less than 0.05 is taken to denote significant relationship.

OBSERVATION & RESULTS

The study was conducted at Sheikh Sayera Khatun Medical College & Hospital, Gopalganj, Bangladesh. 50 patients were included in double blind randomized control study. The number of demand analgesia in 24 hours is 1.56 in Group – M vs 4.2 in Group- C and it is statistically significant (p=0.0002) . Post-operative visual analog score (VAS) in Group-M was 4.64 vs 5 in group – C. But it was highly significant at 2,4,8,12,20 hours and .However, it was not significant at postoperative zero hours, 14, 16,24 hours. Postoperative Ramsay sedation scale (RSS) is 2.16 in group – M, 1.6 in Group – C, this is statistically significant (P=0.0156). The postoperative heart rate in group –M vs Group – C are 85 ± 12.7 and 101 ± 13.9 respectively and it statistically significant (p=0.0002) .The post-operative mean arterial pressure (MAP) is 89 ± 15.7 group- M vs 104 ± 14.3 Group - C which is statically significant (P=0.0012).

Table-1: Age group distribution (N=50)

Age Group	Morphine Group		Control Group	
	No	%	No	%
up to 20yrs	1	4	1	4
21-30	5	20	7	28
31-40	6	24	6	24
41-50	7	28	5	20
51-60	3	12	5	20
above 60	3	12	1	4
Total	25	100	25	100
Mean	41.0 years		39.2 years	
SD	13.8 years		12.6 years	
‘p’ value	0.6835 Not significant			

Table-2: Sex group distribution (N=50)

Sex	Morphine Group		Control Group	
	No	%	No	%
Male	14	56	15	60
Female	11	44	10	40
ToTal	25	100	25	100
'p' value	0.7767 Not significant			

The time for 1st demand analgesia in the postoperative period in Group – M is 13.8 hours and in

Group - C is 1 hour and statistically significant (p=0.00079).

Table-3: Analgesic demand (N=50)

Drug use	Morphine Group		Control Group		P-value
	No.	%	No.	%	
Time for I PT analgesic demand (in hours)	13.8	11.9	1.0	1.0	0.0079 Significant
Number of analgesic demand in 24 hours	1.56	2.31	4.2	2.93	0.0002 Significant
Total NSAID used in 24 hours	0.44	0.51	-	-	-
Inj. Fentanyl used in 24 hours((µg)	1.1	1.94	86	72.6	0.0003 Significant

The number of demand analgesia in 24 hours is 1.56 in Group – M vs 4.2 in Group- C and it is statistically significant (p=0.0002). The rescue analgesia Inj. Fentanyl used in-Groups – M is 1.1 vs 86 in Group – C and it is statistically significant (p=0.0003). The Intraoperative systolic BP was 124 in Group - M and 125 in Group – C and statistically not significant. **Intra operative diastolic B.P:** Intra operative diastolic BP was compared between both groups had (80 group-M and Group – C 82) and p value

as 0.39 and not significant. **Intra operative mean arterial B.P:** The mean arterial pressure is not significant between both groups and group – M had 94 ± 10.8 and in Group – C 96 ± 12.6 and p value 0.5527. But is significant at 90th min (P=0.0262). Probably it is associated with onset of action of IT morphine. **Intra operative pulse Rate:** Intra operative pulse rate in group –M was 90 ± 14 vs 91 ± 16.9 in Group – C and it is statistically not significant.

Table 4: Post-operative VAS (N=50)

Post Op. Vas at	M Group		Control Group		'p' value	Significance
	Mean	SD	Mean	SD		
0 hours	4.64	1.41	5.0	1.41	0.3609	Not Significant
2 hours	4.12	1.2	5.21	0.88	0.0002	Significant
4 hours	3.76	0.88	4.6	0.76	0.0009	Significant
8 hours	3.8	0.76	4.4	0.76	0.0055	Significant
10 hours	3.8	0.71	3.92	0.49	0.2868	Not Significant
12 hours	3.6	0.58	4.04	0.61	0.0137	Significant
14 hours	3.72	0.54	3.76	0.66	0.9177	Not Significant
16 hours	3.84	0.47	3.96	0.45	0.3609	Not Significant
18 hours	3.84	0.47	3.88	0.53	0.8	Not Significant
20 hours	3.84	0.47	4.08	0.76	0.199	Not Significant
22 hours	3.88	0.44	4.4	0.65	0.0017	Significant
24 hours	3.92	0.49	3.84	0.55	0.5704	Not Significant

Post-operative visual analog score (VAS) in Group-M was 4.64 vs 5 in group – C. But it was highly significant at 2,4,8,12,20 hours and However, it was not

significant at postoperative zero hours, 14,16,24 hours. Intrathecal Morphine seems to have a certain lag in onset of analgesia.

Table-5: Post-operative RSS (N=50)

Post Op. Vas at	M Group		Control Group		'p'value	Significance
	Mean	SD	Mean	SD		
0	2.16	0.8	1.6	0.76	0.0156	Significant
2	2.32	0.47	1.56	0.65	0.0001	Significant
4	2.28	0.46	1.56	0.58	0.0001	Significant
6	2.32	0.48	1.68	0.56	0.0002	Significant
8	2.28	0.46	1.68	0.56	0.0003	Significant
10	2.24	0.52	1.88	0.44	0.0124	Significant
12	2.24	0.44	1.92	0.4	0.0113	Significant
14	2.24	0.44	2.0	0.29	0.0281	Significant
16	2.24	0.44	2.04	0.2	0.0437	Significant
18	2.24	0.48	2.04	0.2	0.0107	Significant
20	2.32	0.49	2.04	0.2	0.0051	Significant
22	2.32	0.48	2.04	0.2	0.0107	Significant
24	2.28	0.46	2.04	0.2	0.0219	Significant

Postoperative Ramsay sedation scale (RSS) is 2.16 in group – M, 1.6 in Group – C, This is statistically significant (P=0.0156).

Table-6: Post-Operative Heart Rate (N=50)

Post heart rate at hours	M Group		Control Group		'p'value	Significance
	Mean	SD	Mean	SD		
0	85	12.7	101	13.9	0.0002	Significant
2	80	10.2	100	11.4	0.0001	Significant
4	76	9.8	99	12.2	0.0001	Significant
8	76	11.3	99	10	0.0001	Significant
12	79	11.5	99	11.3	0.0001	Significant
16	78	9.1	100	10.1	0.0001	Significant
20	78	8.2	100	9.6	0.0001	Significant
24	77	8.5	102	8.8	0.0001	Significant

The postoperative heart rate was In group –M vs Group – C are 85 ± 12.7 and 101 ± 13.9 respectively and it statistically significant (p=0.0002) during the post operative period .

Table-7: Post-operative systolic B.P (N=50)

Post operative SBP at hours	M Group		Control Group		'p'value	Significance
	Mean	SD	Mean	SD		
0	116	23.4	138.7	22.2	0.0018	Significant
2	113.0	21.6	135.2	22.2	0.0033	Significant
4	111.3	22.2	140.3	17.5	0.0001	Significant
8	109	22.4	140.2	16.3	0.0001	Significant
12	110.4	20.5	141.5	18.1	0.0001	Significant
16	109.2	19.8	138.4	18.4	0.0001	Significant
20	107.5	18.4	139.4	18.7	0.0001	Significant
24	107.2	17	137.8	17.2	0.0001	Significant

Post-operative systolic BP was 116 ± 23.4 in Group – M vs 138 ± 22 in control Group which is statistically significant p =0.0018.

Table-8: Post-operative Diastolic B.P (N=50)

Post operative DBP at hours	M Group		Control Group		'p' value	Significance
	Mean	SD	Mean	SD		
0	75.4	12.7	87.1	11.7	0.0019	Significant
2	76	13.7	85.8	9.4	0.0145	Significant
4	73.9	13.2	86.6	8.3	0.0001	Significant
8	72.9	12.3	89	9.8	0.0001	Significant
12	73.3	11.1	88.1	9.4	0.0001	Significant
16	72	9.8	87.1	7.5	0.0001	Significant
20	71.2	10.2	86.6	8.4	0.0001	Significant
24	71	9.6	85	6.3	0.0001	Significant

Post-operative Diastolic BP was 75.4 ± 12.7 in group – M vs 87.1 ± 11.7 in control group which is statistically significant $p=0.0019$.

Table-9: Post-operative MAP (N=50)

Post operative MAP at hours	M Group		Control Group		'p' value	Significance
	Mean	SD	Mean	SD		
0	89	15.7	104	14.3	0.0012	Significant
2	88	16.1	102	12.4	0.0049	Significant
4	86	15.9	104	10.1	0.0002	Significant
8	85	15.3	107	10.9	0.0001	Significant
12	86	13.9	106	10.8	0.0001	Significant
16	84	12.4	104	10.1	0.0001	Significant
20	83	12.4	104	10.3	0.0001	Significant
24	83	11.7	103	8.8	0.0001	Significant

The post-operative mean arterial pressure (MAP) is 89 ± 15.7 group- M vs 104 ± 14.3 Group - C which is statistically significant ($P=0.0012$)

Table-10: Complications (N=50)

Complications	Morphine Group		Control Group		%
	No.	%	No.	%	
Nausea	11	44	9	36	
Vomiting	11	44	9	36	
Respiratory Depression	3	12	-	-	
Pruritis	11	44	5	20	
Desaturation	1	4	-	-	
Hypotension	3	12	-	-	
Bradycardia	2	8	-	-	
Total cases with complications	19	76	12	48	
Total cases without complications	6	24	13	52	
'p' value	0.0804				
	Not significant				

There was no statically significant difference in the complication between 2 groups. However Nausea and vomiting was more in the IT Morphine group (11 vs 9). Desaturation, Pruritis, bradycardia and hypotension was also more in the morphine Group .these findings may be clinically relevant although statistical analysis did not reveal any significant difference.

DISCUSSION

Post-operative (VAS) score in Group – M was 4.64 vs 5 in Group – C. But it was highly significant at 2,4,8,12,20 hours and non-significant at post-operative

0,14,16,24 hours. Intrathecal morphine has superior post operative analgesia effect .Gwartz KH ,Young JV, Byers RS, Alley C, Levin K, Walker SG, Stoelting RK found in their retrospective study intrathecal morphine analgesia was superior for acute postoperative pain in 5969 surgical patients studied at Indian University Hospital undergoing major urologic, orthopedic, general/vascular thoracic and gynecology surgeries [3-7]. The findings in our study are in agreement with this study. Jean-Michael Devys, Anne Mora, Benoit Plaud et al in their study found IT morphine 0.4mg I 60 adult patient undergoing major abdominal surgery produce VAS scores that were lower in the IT morphine group for the first 48 hours [8]. This is totally in agreement

with finding of this study. The number of demand analgesia in 24 hours is 1.56 in group – M vs 4.2 in group – C and it is statically significant ($p=0.0002$). It is Fentanyl used in group - M is 1.1 vs 86 in group – C and it is statically significant ($p=0.0003$). Andrew et al studied the efficacy and safety of low dose intrathecal morphine for post operative analgesia in children. The time for demand analgesia by patient required Opioid administration (parental or oral) was approximately 8 hours .our study has similar findings established the efficacy of IT morphine. Intra operatively SBP, DBP, MAP, HR, SaO₂ there was no difference between both Groups M and C. Post operatively group – M demonstrated significantly stable hemodynamics due to superiors and stables pain control. ASK Kwan , BB.Lee, T.Brake et al in their study used 0.2 mg IT morphine to 2.2ml of hyperbaric bupivacaine in patients undergoing hip surgeries no alterations in hemodynamics both intra-operative and post operative period [9]. The finding in our study agree with these conclusions. Nausea and vomiting was more in IT Morphine group (11 vs 9). Desaturation, Pruritus, bradycardia and hypotension was also more in Group-M although these findings may be clinically relevant but statistical did not reveal any significant difference. Gyan CG *et al.*, 1979 and Davies GK *et al.*, 1980 reported respiratory depression following spinal morphine [10-12] in our study 2 patient with hypoventilation and 1 patient developed desaturation but were easily managed by oxygen supplementation. Reiz and Westberg 1980 and Yaksh TL 1981 and samii j, chanin M and Viars P 1981 reported pruritus and urinary retention after intrathecal opioids, Our study recorded pruritis but urinary retention could not be assessed since all patients continued to have their bladder catheterized during the study period [11, 12, 14]. Ganesh A,K.M.A Cucchiario studied the effect of low dose (4-5 μ g/kg) intrathecal morphine and found the incidence of Nausea or vomiting pruritus and urinary retention was 32%,37% and 6% respectively [15]. The findings in our study are in concurrence with these studies.

CONCLUSION

Intrathecal morphine produced better postoperative analgesia and sedation. Intrathecal morphine group demonstrated lesser amounts of analgesic and rescue analgesic requirement during the postoperative period. Intrathecal morphine produced better hemodynamic stability in the postoperative period. Intrathecal morphine produced side effects in the form of nausea, vomiting, hypotension and bradycardia but not statistically significant.

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