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INTRATHECAL MIDAZOLAM INCREASES THE ANALGESIC EFFECTS OF SPINAL BLOCKADE WITH BUPIVACAINE IN PATIENTS UNDERGOING HAEMORRHOIDECTOMY

Anaesthesiology

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ABSTRACT

BACKGROUND AND OBJECTIVES: After haemorrhoidectomy, many patients require parenteral oral opioids and/or nonsteroidal antiinflammatory drugs (NSAIDs) for analgesia.The use of opioids in intrathecal or epidural anaesthesia has become popular to optimize postoperative analgesia. However, opioid-induced side effects, such as respiratory depression, nausea, vomiting, urinary retention and pruritus, limit their use.The purpose of our study was to assess the effects of intrathecal midazolam as an adjunct to intrathecal bupivacaine after haemorrhoidectomy. **METHODOLOGY:** Total 60 patients undergoing electivehaemorrhoidectomy under spinal anaesthesia was selected randomly allocated into two groups of 30 patients each by a computer generated randomization method.

1. Group 2 received 1.5 ml of 0.5% bupivacaine plus 0.2 ml of 0.5% preservative-free midazolam
2. The control group received 1.5 ml of 0.5% heavy bupivacaine plus 0.2 ml of 0.9% saline intrathecally.

Institutional Ethics Committee approval was taken prior to commencement of the study. This prospective randomized study was conducted atMeenakshi Medical College Hospital and Research Institute. Parameters such as Heart rate (HR), Systolic blood pressure (SBP),Diastolic blood pressure (DBP),Mean arterial pressure (MAP), Saturation (Spo2) , Duration of effective analgesic time from the spinal anaesthesia; visual analogue scales (VAS) at first analgesia; and total consumption of analgesics in the 24 h after spinal anaesthesia was recorded. **RESULT:** There were nostatistical significant differences between the study groups in means of systolic blood pressure, diastolic blood pressure, heartrate, respiratoryrate, mean arterial pressure,SPO2 taken but there was significant difference in duration of analgesia was longer in bupivaine-midazolam group. **CONCLUSION:** The present study there was significant difference in VAS on analgesic administration in two groups. VAS score is better in midazolam group compared to control group. The duration of analgesia was longer in bupivaine-midazolam groupcompared with bupivacaine group ,which was statistically significant.

KEYWORDS

Anaesthetic Techniques, Spinal; Analgesia, Postoperative, Anaesthetics Local, Bupivacaine; Hypnotics Benzodiazepine, Intrathecal Midazolam; Surgery, Haemorrhoidectomy

INTRODUCTION

After haemorrhoidectomy, many patients require parenteral oral opioids and/or nonsteroidal antiinflammatory drugs (NSAIDs) for analgesia. The use of opioids in intrathecal or epidural anaesthesia has become popular to optimize postoperative analgesia. However, opioid-induced side effects, such as respiratory depression, nausea, vomiting, urinary retention and pruritus, limit their use. The purpose of our study was to assess the effects of intrathecal midazolam as an adjunct to intrathecal bupivacaine after haemorrhoidectomy.

One of the major encounters in perioperative care after haemorrhoidectomyis the postoperative analgesia. Due to pain, the patients undergo physiological and psychological retorts. The majority of these are damaging to postoperative outcome. Insufficient relief of postoperative pain causes several issues. Some of them can be prolonged recovery, increase in the duration hospital stay, and surge in the hospital cost. The modern day anaesthesiologists should consider it their responsibility to ensure patient comfort throughout the preoperative, intraoperative, and postoperative period.The anaesthesiologists are perioperative physicians.

There are several methods to provide postoperative analgesia. Among them intrathecal opioids and nonopioids as adjuncts in spinal anesthesia are mostly recognised. The intrathecal opioids often have related dose related adverse effects. So,the nonopioids such as ketamine, clonidine, neostigmine, magnesium sulfate, midazolam have became popular adjuncts for postoperative analgesia. It is found that intrathecal or epidural administration of midazolam yields a dosedependent inflection of spinal nociceptive processing in animals as well ashumans. But not associated with neurotoxicity, respiratory depression, or sedation.[1]Subarachnoidanesthesia is considered as one of the well-knownneuraxial block techniques existing currently. Subarachnoid anesthesia provides numerous benefits when compared to general anesthesia.

The benefits include fall in intraoperative loss of blood, fall in the postoperative occurrence of thromboembolic phenomena, and declining pain in the early period postoperatively.[2] Spinal anesthesia is used in a variety of lower abdominal, urologic, orthopedic, and minor vascular procedures. It is easy to perform and provides rapid onset and effective sensory and motor block.[3]The concept of spinal anesthesia is unique and unparalleled in a way that a small mass of drug, virtually devoid of systemic pharmacological effects can produce profound surgical anesthesia. A single intrathecal injection with local anesthetic is used for effective sensory and motor blockade.[4]

METHODOLOGY

This prospective randomized study was conducted at Meenakshi Medical College Hospital and Research Institute.

TYPE OF STUDY

Prospective study

STUDY PLACE

Meenakshi Medical College Hospital and Research Institute.

PERIOD OF STUDY

JUNE-2019 to JUNE-2020.

STUDY POPULATION

The study will be conducted prospectively in 60 patients of 18 to 60 years of age scheduled patients undergoing elective haemorrhoidectomy under spinal anaesthesia at Meenakshi medical college hospital and research centre.

SAMPLE SIZE

60 patients were randomly allocated into two groups of 30 patients each by a computer generated randomization method.

INCLUSION CRITERIA

- ASAgrades I or II.
- Ages between 18 and 60 years of either sex.
- Patient undergoing elective haemorrhoidectomy under spinal anaesthesia

- Hemodynamically stable

EXCLUSION CRITERIA

a. Patient refusal
b. Patients with ASA physical status III or more.
c. Patients with anticipated difficult intubation
d. Patients posted for emergency surgery.
e. Patients on any opioid or any sedative medication in the week prior to the surgery.
f. Patients who are known allergic to any of the test drugs..

DATA COLLECTION TOOLS AND PROCEDURE

60 patients were randomly allocated into two groups of 30 patients each by a computer generated randomization method.

Group 1 received 1.5 ml of 0.5% bupivacaine plus 0.2 ml of 0.5% preservative-free midazolam

Group 2 (Control) received 1.5 ml of 0.5% heavy bupivacaine plus 0.2 ml of 0.9% saline intrathecally

Institutional Ethics Committee approval was taken prior to commencement of the study. Total 60 patients undergoing elective haemorrhoidectomy under spinal anaesthesia was selected randomly and were divided into two group 1received 1.5 ml of 0.5% bupivacaine plus 0.2 ml of 0.5% preservative-free midazolam and the control group received 1.5 ml of 0.5% heavy bupivacaine plus 0.2 ml of 0.9% saline intrathecally. Parameters such as Heart rate (HR), Systolic blood pressure (SBP),Diastolic blood pressure (DBP),Mean arterial pressure (MAP), Saturation (Spo2) , Duration of effective analgesic time from the spinal anaesthesia; visual analogue scales (VAS) at first analgesia; and total consumption of analgesics in the 24 h after spinal anaesthesia was recorded with rescue analgesia with oral parcetamol 500mg tablet.

STATISTICAL ANALYSIS

Data were entered in Microsoft Excel Sheet. Descriptive statistics were reported as mean (SD) for continuous variables, frequencies (percentage) for categorical variables. Chi-Square at 5% level of significance was used to find statistical significance. Fischer's exact test is when expected cell count is less than 5. Data were statistically evaluated with IBM SPSS Statistics for Windows, Version 20.0., IBM Corp., Chicago, IL.

RESULTS

Table 1: Age Distribution of Study Groups

Group	Number	Mean	S.D	t	df	P value
Group-1	30	37.267	9.18	0.538	58	0.592
Group-2	30	38.567	9.51			

The mean age in group 1 was 37.26 and Mean age in group 2 was 38.56.The two groups were comparable in means of age as P value is more than 0.05.Hence it shows that baseline character in means of age is same for both the groups.

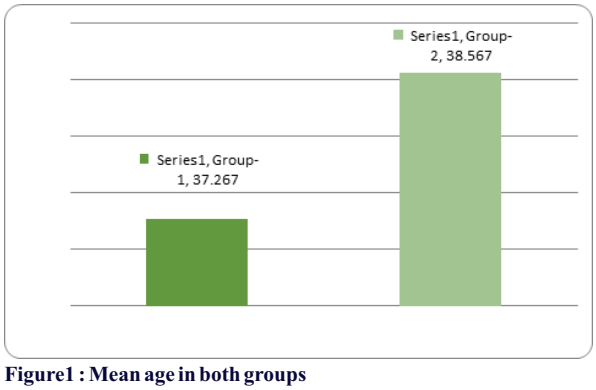

Figure1 : Mean age in both groups

Table 2: Sex Distribution of Study Groups

Group	Male	Female	Total	df	CHI Square	P value
Group-1	15	15	30	3	1.506	0.681
Group-2	14	16	30			
Total	29	31	60			

In both the groups distribution of males is same. The two groups are comparable with sex as P value is more than 0.05

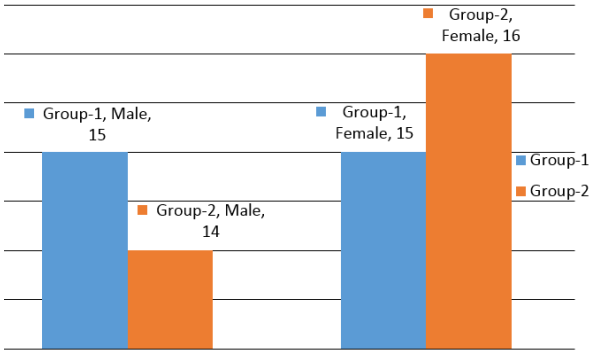

Figure 2: Sex Distribution of Study Groups

Table 3: Height wise Distribution of Study Groups

Group	Number	Mean	S.D	t	df	P value
Group-1	30	157.67	8.05	0.310	58	0.757
Group-2	30	157.10	8.57			

The mean Height in group 1 was 157.67 and in group 2 it was 157.10.The two groups are comparable with respect to height.(P>0.05)

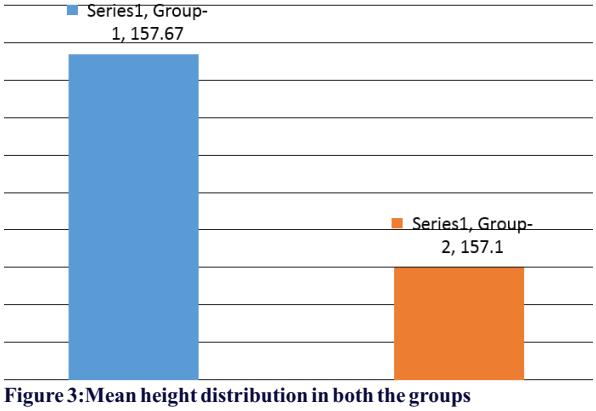

Figure 3:Mean height distribution in both the groups

Table 4: Weight wise Distribution of Study Groups

Group	Number	Mean	S.D	t	df	P value
Group-1	30	68.06	13.25	0.00	58	1.0
Group-2	30	68.06	12.27			

The two groups had similar means .Hence we have got p value as1.0.But the standard deviation of two groups is different but not statistically different .

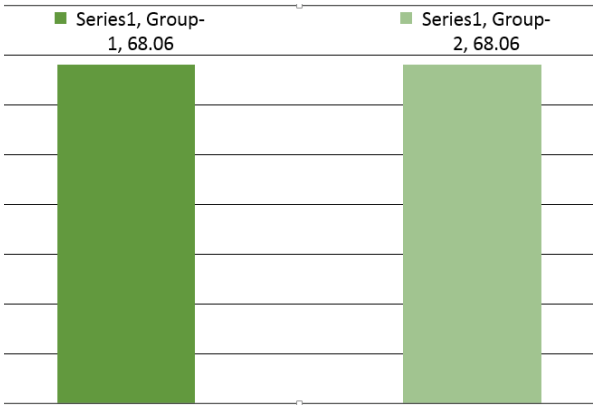

Figure 4: Weight wise Distribution of Study Groups

Table 5: Duration of Surgery (Minutes)

Group	Number	Mean	S.D	t	df	P value
Group-1	30	25.66	3.88	0.163	58	0.87
Group-2	30	25.50	4.01			

The mean duration of surgery in group 1 is 25.66 minutes and standard deviation is 3.88.The The mean duration of surgery in group 2 is 25.50 minutes and standard deviation is 4.01.The two groups duration of

surgery do not differ statistically.

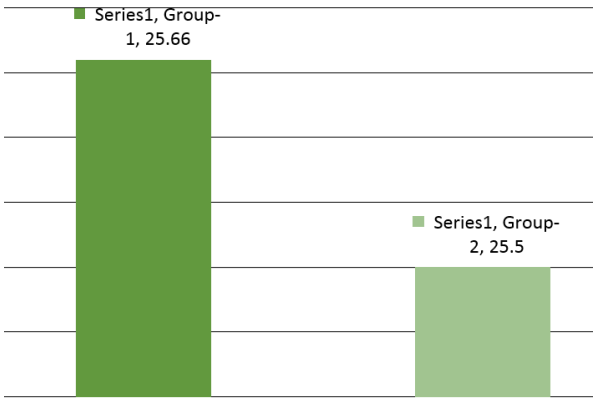

Figure 5: Mean Duration of Surgery (Minutes)

Table 6: VAS at first pain medication (mm)

Group	Number	Mean	S.D	t	df	P value
Group-1	30	29	6.07	5.4	58	<0.0001
Group-2	30	36.67	4.79			

There was significant difference in VAS on analgesic administration in two groups and P value<0.0001.In group 1 mean was 29 and in group 2 mean was 36.67mm.Standard deviation of group 1 was 6.07 and standard deviation of group 2 was 4.79.

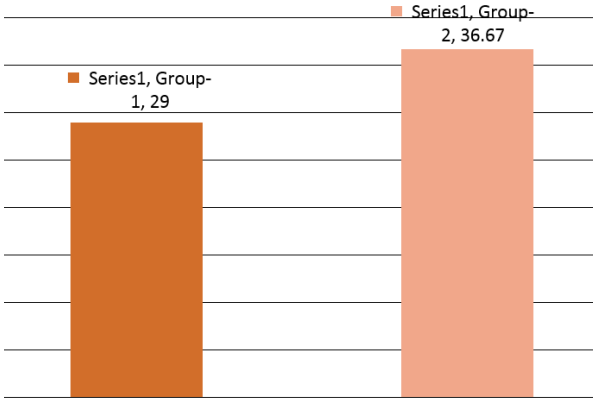

Figure 6: VAS at first pain medication (mm)

Table 7: Time to first pain medication(hrs)

Group	3	4	5	6	Total	X2	p
Group-1	0	0	13	17	30	60	0.0001
Group-2	14	16	0	0	30		

In group 1it took 5 hours for 13 patients and 6 hrs for 17 patients to take first pain medication while in group 2 it took 3 hours for 14 patients and 4 hours for 16 patients to take firstpain medication.The two groups differ statistically with respect to time to first pain medication(P value<0.0001)

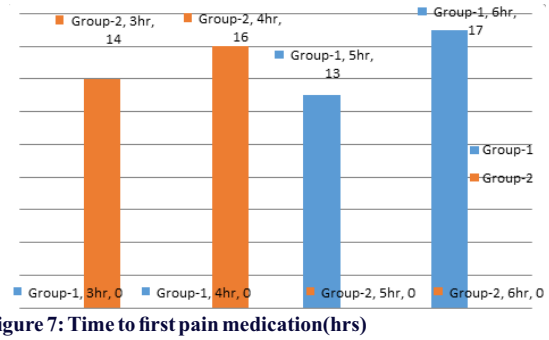

Figure 7: Time to first pain medication(hrs)

Table 8: No. of Oral Paracetamol in 24hrs

Group	2	3	4	Total	X2	P value
Group-1	17	13	0	30	37.39	0.0001
Group-2	0	10	20	30		

In group 1, 17 patients took 2 paracetamol in 24hours,13 patients took 3 paracetamol in 24 hours .In group2 ,10 patients took 3 tablets in 24 hoursand 20 patiens took 4 paracetamol in 24 hours.The two groups statistically differ with respect to no of oral paracetamol in 24 hours.P value is 0.0001.

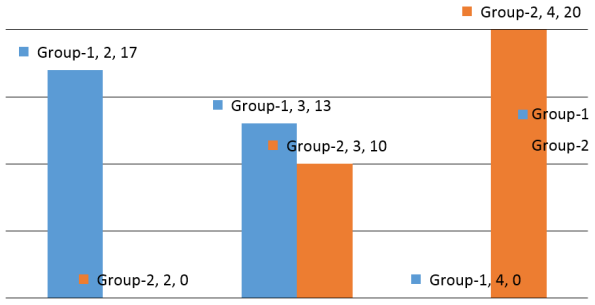

Figure 8: No. of Oral Paracetamol in 24hrs

Table 9: Time of first self voiding(hrs)

Group	2	3	Total	X2	df	P value
Group-1	15	15	30	1.086	1	0.297
Group-2	19	11	30			
Total	34	26	60			

The two groups do not differ statistically with respect to time of first self voiding(hrs).P value is 0.297.

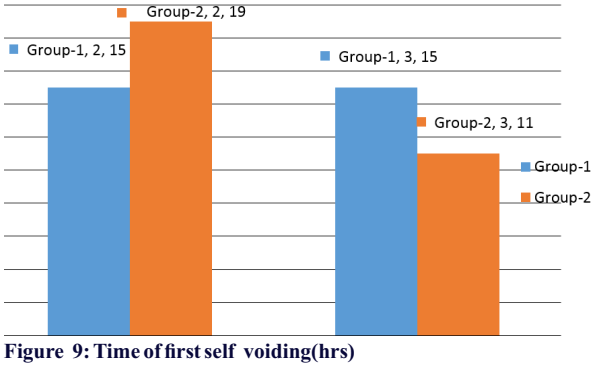

Figure 9: Time of first self voiding(hrs)

Table 10: Systolic blood pressure in both the groups

Time of Assessment	Mean + SD		df	t value	P value
	Group-1	Group-2			
0 min	117+10.45	117+10.53	58	0.36	0.62
5 min	118+10.36	117+10.87	58	0.046	0.92
10 min	118+10.01	118+10.83	58	0.08	0.94
15 min	118+10.38	118+11.01	58	0.12	0.90
20 min	118+10.39	118+11.03	58	0.18	0.92
30 min	118+10.42	118+11.07	58	0.32	0.66
1 hr	118+10.47	117+10.86	58	0.01	0.99
2 hr	117+10.04	118+10.09	58	0.33	0.64
4 hr	117+10.03	118+11.09	58	0.39	0.79
6 hr	117+10.01	118+11.19	58	0.48	0.83
12 hr	117+10.01	118+11.10	58	0.68	0.65
24 hr	117+9.96	118+11.07	58	1.04	0.52

In group 1, the mean systolic blood pressure ranged from 117 ±9.96 to 118 ±10.42mm of Hg. In group 2, the mean systolic blood pressure ranged from 117 ±10.53 to 118 ±11.10 mm of Hg. The statistical analysis by independent t test showed that there was no significant difference in systolic blood pressure between the two groups ($p > 0.05$) in different time of assessment

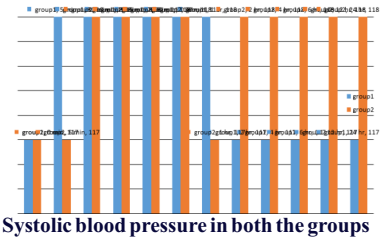

Figure 10: Systolic blood pressure in both the groups

Table 11: Diastolic Blood Pressurein both the groups

Time of Assessment	Mean + SD		df	t value	P value
	Group-1	Group-2			
0 min	76+7.22	77+6.8	58	0.26	0.8
5 min	76+7.52	77+6.74	58	0.71	0.38
10 min	76+7.07	77+6.72	58	0.82	0.31
15 min	76+7.08	77+6.76	58	0.83	0.30
20 min	76+7.09	77+6.78	58	0.84	0.29
30 min	76+7.10	77+6.85	58	0.27	0.79
1 hr	76+7.03	77+6.66	58	0.54	0.52
2 hr	76+7.06	77+6.82	58	0.34	0.72
4 hr	76±7.05	77±6.84	58	0.36	0.73
6 hr	76+7.15	77+6.73	58	0.37	0.75
12 hr	76+6.9	77+6.92	58	0.37	0.75
24 hr	76+6.9	77+6.67	58	0.36	0.74

In group 1, the mean diastolic blood pressure ranged from 76 ±7.03to 77 ±7.52 of Hg. In group 2, the mean diastolic blood pressure ranged from 77 ±6.66to 77 ±6.92mm of Hg. The statistical analysis by independent t test showed that there was no significant difference in diastolic blood pressure between the two groups ($p > 0.05$).

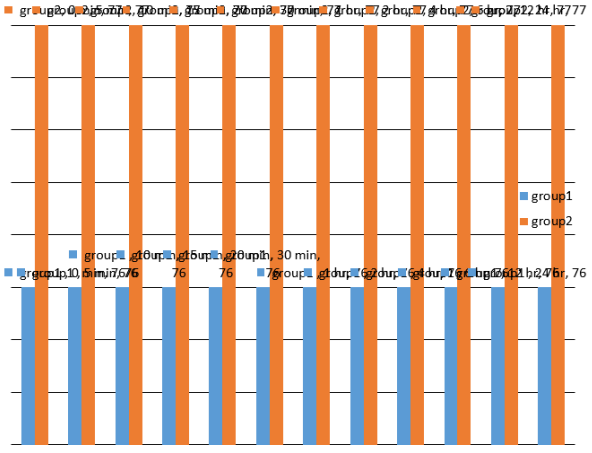

Figure 11: Diastolic Blood Pressurein both the groups

Table 12: Mean Arterial pressure in both the groups

Time of Assessment	Mean + SD		df	t value	P value
	Group-1	Group-2			
0 min	83.60+4.63	83.77+4.02	58	0.88	0.187
5 min	88.70+7.65	88.33+7.53	58	0.85	0.206
10 min	89.71+7.85	89.68+7.55	58	0.75	0.216
15 min	89.73+8.01	89.70+7.58	58	0.65	0.221
20 min	89.75+8.03	89.72+7.8	58	0.60	0.385
30 min	89.78+8.05	89.74+7.9	58	0.56	0.410
1 hr	88.70+7.65	88.76+7.92	58	0.54	0.526
2 hr	88.56+7.15	88.78+7.76	58	0.52	0.610
4 hr	88.40+7.25	88.80+7.54	58	0.68	0.620
6 hr	88.38+7.05	88.82+7.52	58	0.72	0.316
12 hr	88.34+6.95	88.84+7.50	58	0.82	0.220
24 hr	88.32+6.75	88.86+7.49	58	0.84	0.190

The two groups do not differ statistically in the mean arterial pressure at different times as P value is more than 0.05.

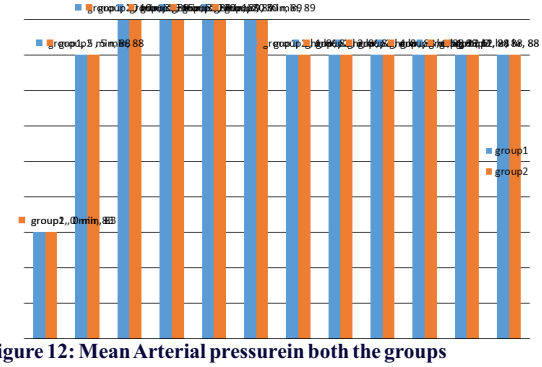

Figure 12: Mean Arterial pressurein both the groups

Table 13: Heart rate in both the groups

Time of Assessment	Mean + SD		df	t value	P value
	Group-1	Group-2			
0 min	77+7.68	78+7.4	58	1.03	0.18
5 min	77+7.66	78+7.0	58	0.91	0.23
10 min	77+7.68	78+7.0	58	1.02	0.22
15 min	76+7.0	78+7.0	58	1.03	0.17
20 min	76+6.8	78+7.2	58	1.03	0.18
30 min	76+6.6	78+7.4	58	1.04	0.16
1 hr	90+6.53	82.67+5.90	58	0.99	0.885
2 hr	77+7.0	78+7.0	58	0.79	0.32
4 hr	77+6.8	78+7.0	58	0.99	0.22
6 hr	77+6.6	78+7.0	58	1.05	0.19
12 hr	76+6.0	78+7.0	58	1.49	0.11
24 hr	77+7.0	78+7.0	58	1.09	0.19

The two groups do not differ statistically in heart rate at different times of assessment as P value is more than 0.05.

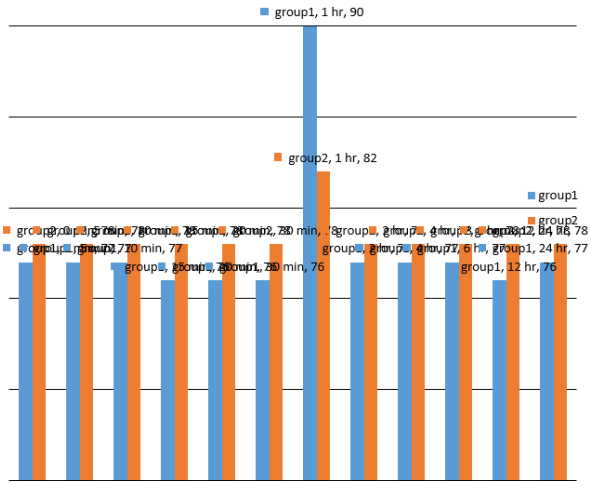

Figure 13: Heart rate in both the groups

Table 14: SpO2 in both the groups

Time of Assessment	Mean + SD		df	t value	P value
	Group-1	Group-2			
0 min	99+0.56	99+0.49	58	0.01	0.99
5 min	99+0.47	99+0.50	58	1.8	0.12
10 min	99+0.48	99+0.70	58	1.9	0.23
15 min	99+0.49	99+0.50	58	0.39	0.75
20 min	99+0.51	98+0.50	58	0.60	0.64
30 min	99+0.54	98+0.50	58	2.09	0.10
1 hr	99+0.50	98+0.50	58	0.19	0.88
2 hr	99+0.48	99+0.47	58	0.20	0.85
4 hr	99+0.48	99+0.47	58	0.20	0.85
6 hr	99+0.49	99+0.47	58	2.45	0.09
12 hr	99+0.57	99+0.46	58	2.09	0.05
24 hr	99+0.48	99+0.46	58	3.58	0.05

The two groups do not differ statistically in SPO2 at different times of assessment as P value is more than 0.05.

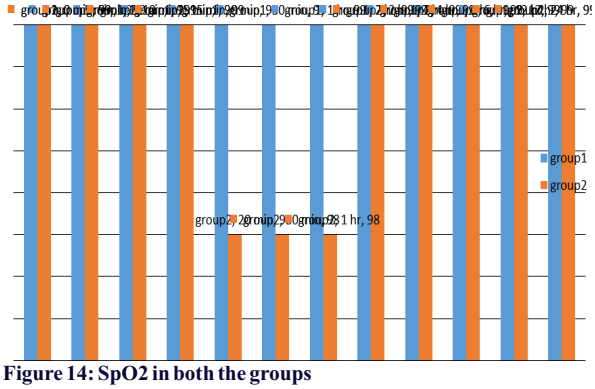

Figure 14: SpO2 in both the groups

Table 15: Respiratory Rate in both the groups

Time of Assessment	Mean + SD		df	t value	P value
	Group-1	Group-2			
0 min	14.17+1.577	13.70+1.745	58	1.087	1.0
5 min	14.16+1.57	13.70+1.745	58	1.087	1.0
10 min	14.16+1.57	13.70+1.74	58	1.087	1.0
15 min	14.16+1.57	13.70+1.74	58	1.087	1.0
20 min	15.05+1.58	15.04+1.56	58	2.086	0.86
30 min	15.15+1.57	15.14+1.55	58	2.087	0.87
1 hr	15.14+1.56	15.13+1.54	58	2.087	0.87
2 hr	15.05+1.58	15.04+1.56	58	2.086	0.86
4 hr	14.16+1.57	13.70+1.74	58	1.087	1.0
6 hr	14.16+1.57	13.70+1.75	58	1.087	1.0
12 hr	14.15+1.57	13.60+1.74	58	1.087	1.0
24 hr	14.14+1.57	13.50+1.72	58	0.98	0.9

The two groups do not differ statistically in Respiratory rate at different times of assessment as P value is more than 0.05.

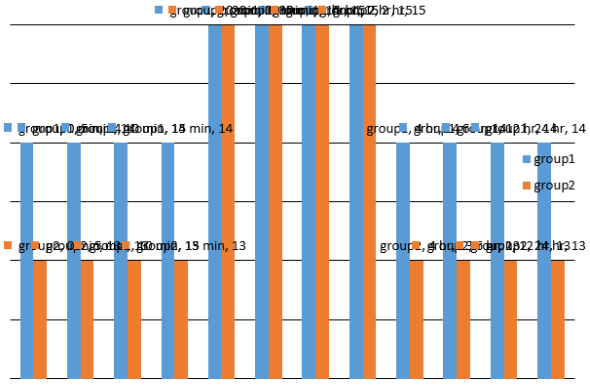

Figure 15: Respiratory Rate in both the groups

DISCUSSION

Patients undergoing elective haemorrhoidectomy admitted in Meenakshi medical College allocated to two groups.60 patientsundergoing elective haemorrhoidectomy under spinal anaesthesia were randomly allocated into two groups of 30 patients each by a computer generated randomization method.

1. Group received 1 ml of 0.5% bupivacaine plus 0.2 ml of 0.5% preservative-free midazolam
2. The control group received 1 ml of 0.5% heavy bupivacaine plus 0.2 ml of 0.9% saline intrathecally.

Parameters such as Heart rate (HR), Systolic blood pressure (SBP),Diastolic blood pressure (DBP),Mean arterial pressure (MAP), Saturation (Spo2), Duration of effective analgesic time from the spinal anaesthesia and total consumption of analgesics in the 24 h after spinal anaesthesia was recorded.

Age distribution between both the groups

The mean age in group 1 was 37.26 and Mean age in group 2 was 38.56.The two groups were comparable in means of age as P value is more than 0.05.Hence it shows that baseline character in means of age is same for both the groups.

Comparison with other studies

	Present study	Nasreenetal[78]	Kojjarboetal[79]
Group 1 mean age	37.26±9.18	32.5+2.47	33.2+9.29
Group 2 mean age	38.56±9.51	33.1+1.46	33.65+9.34
P value	0.59	0.30	>0.05

The above two studies results and our study results are same with respect to age distribution as in all the above studies both rouos age are comparable.

Sex distribution

In both the groups distribution of males is same.The two groups are comparable with sex as P value is more than 0.05

Height distribution

The mean Height in group 1 was 157.67 and in group 2 it was 157.10.The two groups are comparable with respect to height.(P>0.05)

Weight distribution

The two groups had similar means .Hence we have got p value as1.0.But the standard deviation of two groups is different but not statistically different

Duration of surgery

The mean duration of surgery in group 1 is 25.66 minutes and standard deviation is 3.88.The The mean duration of surgery in group 2 is 25.50 minutes and standard deviation is 4.01.The two groups duration of surgery do not differ statistically.

VAS at first pain medication (mm)

There was significant difference in VAS on analgesic administration in two groups and P value<0.0001.In group 1 mean was 29 and in group 2 mean was 36.67mm.Standard deviation of group 1 was 6.07 and standard deviation of group 2 was 4.79.

Duration of analgesia

In group 1it took 5 hours for 13 patients and 6 hrs for 17 patients to take first pain medication while in group 2 it took 3 hours for 14 patients and 4 hours for 16 patients to take firstpain medication.The two groups differ statistically with respect to time to first pain medication(P value<0.0001) The duration of analgesia was longer in bupivaine-midazolam group compared with bupivacaine group ,which was statistically significant.

Studies	P value	Inference
Present study	0.0001	Significant
Gulec et al[80]	0.01	Significant
Shaikh et al[81]	0.01	Significant
Nishiyama et al[82]	0.01	Significant
Batra et al [83]	0.01	Significant

Hence the above studies have similar findings like our study.

No. of Oral Paracetamol in 24hrs

In group 1, 17 patients took 2 paracetamol in 24hours,13 patients took 3 paracetamol in 24 hours .In group2 ,10 patients took 3 tablets in 24 hoursand 20 patiens took 4 paracetamol in 24 hours.The two groups statistically differ with respect to no of oral paracetamol in 24 hours.P value is 0.0001.

	P value	Inference
Present study	0.0001	Significant
Nasreen etal1	0.001	Significant
Jarboetal2	0.05	Significant

The above two studies showed findings consistent with our study .The two groups do not differ statistically with respect to time of first self voiding(hrs).P value is 0.297.

Haemodynamic parameters

Systolic Blood pressure

In group 1, the mean systolic blood pressure ranged from 117 ±9.96 to 118 ±10.42mm of Hg. In group 2, the mean systolic blood pressure ranged from 117 ±10.53 to 118 ±11.10 mm of Hg. The statistical analysis by independent t test showed that there was no significant difference in systolic blood pressure between the two groups ($p > 0.05$) in different time of assessment.

Diastolic Blood pressure

In group 1, the mean diastolic blood pressure ranged from 76 ±7.03to 77 ±7.52 of Hg. In group 2, the mean diastolic blood pressure ranged from 77 ±6.66to 77 ±6.92mm of Hg. The statistical analysis by independent t test showed that there was no significant difference in diastolic blood pressure between the two groups ($p > 0.05$).

Mean Arterial Pressure

The two groups do not differ statistically in the mean arterial pressure at different times as P value is more than 0.05.

Heart rate

The two groups do not differ statistically in heart rate at different times of assessment as P value is more than 0.05.

Respiratory rate

The two groups do not differ statistically in Respiratory rate at different times of assessment as P value is more than 0.05.

SPO2

The two groups do not differ statistically in SPO2 at different times of assessment as P value is more than 0.05.

INFERENCE

There were no statistical significant differences between the study groups in means of systolic blood pressure, diastolic blood pressure ,heart rate, respiratory rate ,mean arterial pressure,SPO2 taken at 0min ,5min, 10min ,15min ,20min ,30min, 1hr,2hr,4hrs,6hrs,12hs,24hrs as P value is more than 0.05.

Comparison with other studies for haemodynamic parameters.

Studies	P value	Inference
Present study	>0.05	Not significant
Nasreen etal78	>0.05	Not significant
Koj jarboetal79	>0.05	Not significant
Sheik etal81	>0.05	Not significant
Badraetal83	>0.05	Not significant

These findings correlates with our study in which haemodynamic variables were comparable between the study groups. Opioids, though very effective in perioperative pain management, may be associated with distressing side effects like pruritis, nausea-vomiting, and respiratory depressionIn contrast none of the participants had postoperative nausea,vomiting,urinary retention and postoperative sedation

CONCLUSION

There was significant difference in VAS on analgesic administration in two groups. VAS score is better in midazolam group compared to control group. The duration of analgesia was longer in bupivaine-midazolam group compared with bupivacaine group ,which was statistically significant.

SUMMARY

The present study is a randomized controlled trial conducted among 60 patients of 18 to 60 years of age undergoing elective haemorrhoidectomy under spinal anaesthesia at Meenakshi medical college hospital and research centre.60 patients were randomly allocated into two groups of 30 patients each by a computer generated randomization method.Group 1 received 1.5 ml of 0.5% bupivacaine plus 0.2 ml of 0.5% preservative-free midazolam and the control group received 1.5 ml of 0.5% heavy bupivacaine plus 0.2 ml of 0.9% saline intrathecally.

There was significant difference in VAS on analgesic administration in two groups.VAS score is better in midazolam group compared to control group. The duration of analgesia was longer in bupivaine-midazolam group compared with bupivacaine group ,which was statistically significant. It is found from the previous literature that intrathecal or epidural administration of midazolam yields a dose-dependent inflection of spinal nociceptive processing in animals as well ashumans. But not associated with neurotoxicity, respiratory depression, or sedation.Many studies to be conducted in future to prove the efficacy of midazolam over opioids as opioids result in many adverse effects.

REFERENCES

1. Kulkarni M, Kurdi M, Itagimath S, Sujatha DA, Muralidhar MK. The role of intrathecal midazolam as an adjunct to bupivacaine in providing post operative pain relief. 2012;1(4):231–4.
2. Ajam AAM, Guri RJ. Effect of Midazolam on Bupivacaine Action in Intrathecal Anesthesia. MedJBabylon. 2018;43–7.
3. Ebied RS, Ali MZ, Boules ML, Samhan YM. Does intrathecal midazolam improve hyperbaric bupivacaine – fentanyl anesthesia in elderly patients ? 2015;602–7.
4. Tiwary V, Punetha S. Characteristics of Block and Post-Operative Analgesia of Low Dose Intrathecal Fentanyl and Midazolam Combined With Hyperbaric 0 . 5 % Bupivacaine in Patients Undergoing Lower Limb Orthopaedic Surgeries. Int J Res Rev. 2020;7(January):433–8.
5. Shadangi BK, Garg R, Pandey R, Das T. Effects of intrathecal midazolam in spinal anaesthesia: A prospective randomised case control study. Singapore Med J 2011;52:432-5
6. Gupta A, Kamat H, Kharod U. Efficacy of intrathecal midazolam in potentiating the analgesic effect of intrathecal fentanyl in patients undergoing lower limb surgery. 2015;379–83.
7. Safari F, Dabbagh A, Sharifnia M. The effect of adjuvant midazolam compared with fentanyl on the duration of spinal anesthesia with 0.5% bupivacaine in opium abusers. Korean journal of anesthesiology 2012;63(6):521-6.
8. Tamsen A, Gordh T. Epidural clonidine produces analgesia. Lancet 1984;2:231-2.
9. Prakash S, Joshi N, Gogia AR, Prakash S, Singh R. Analgesic efficacy of two doses of intrathecal midazolam with bupivacaine in patients undergoing cesarean delivery. RegAnesth Pain Med 2006;31:2216.
10. Crawford ME, Jensen FM, Toftdhal DB, Madesen JB. Direct spinal effect of intrathecal and extradural midazolam on visceral noxious stimulation in rabbits. Br J Anaesth 1993;70:6426.
11. Serrao JM, Marks RL, Morley SJ, Goodchild CS. Intrathecal midazolam for the treatment of chronic mechanical low back pain: A controlled comparison with epidural steroid in a pilot study. Pain 1992;48:512.
12. Nishiyama T, Hanaoka K. Midazolam can potentiate the analgesic effects of intrathecal bupivacaine on thermal or inflammatoryinduced pain. AnesthAnalg 2003;96:138691.
13. Goodchild CS, Guo Z, Musgreave A, Gent JP. Antinociception by intrathecal midazolam involves endogenous neurotransmitters acting at spinal cord delta opioid receptors. Br J Anaesth 1996;77:75863.
14. Rudra P, Rudra A. Comparison of intrathecal fentanyl and midazolam for prevention of nausea – Vomiting during caesarean delivery under spinal anaesthesia. Indian J Anaesth 2004;486:4614.
15. Nishiyama T, Hanaoka K. Midazolam can potentiate the analgesic effects of intrathecal bupivacaine on thermal- or inflammatoryinduced pain. AnesthAnalg. 2003;96:1386–91. http://dx.doi. org/10.1213/01.ANE.0000057606.82135.7D
16. Gupta A, Prakash S, Deshpande S, et al. The effect of intrathecal midazolam 2.5 mg with hyperbaric bupivacaine on postoperative pain relief in patients undergoing orthopaedic surgry. Internet J Anesthesiol. 2007;14:11,
17. Agrawal N, Usmani A, Sehgal R, et al. Effects of intrathecal midazolam bupivacaine combination on postoperative analgesia. Indian J Anaesth. 2005;49:37–9
18. Prakash S, Joshi N, Gogia AR, et al. Analgesic efficacy of two doses of intrathecal midazolam with bupivacaine in patients undergoing cesarean delivery. RegAnesth Pain Med. 2006;31:221–6. http://dx.doi.org/10.1097/00115550-200605000-00008,
19. Karbasfrushan A, Farhadi K, Amini-Saman J, et al. Effect of intrathecal midazolam in the severity of pain in cesarean section: a randomized controlled trail. Iran Red Crescent Med J. 2012;14:276–82.
20. Sanad H, Abdelsalam T, Hamada M, et al. Effects of adding magnesium sulphate, midazolam or ketamine to hyperbaric bupivacaine for spinal anaesthesia in lower abdominal and lower extremity surgery. Ain Shams J Anesthesiol. 2010;3:43–52
21. Chattopadhyay A, Maitra S, Sen S, et al. A study to compare the analgesic efficacy of intrathecal bupivacaine alone with intrathecal bupivacaine midazolam combination in patients undergoing elective infraumbilical surgery. Anesthesiol Res Pract. 2013; Article ID 567134:1–5. doi: 10.1155/2013/567134.
22. Bharti N, Madan R, Mohanty PR, et al. Intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia, ActaAnaesthesiologicaScandinavica. 2003;47:1101–5. http://dx.doi. org/10.1034/j.1399-6576.2003.00186.x
23. Kim MH, Lee YM. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy. Br J Anaesth. 2001;86:77–9. http://dx.doi.org/10.1093/bja/86.1.77
24. Yegin A, Sanli S, Dosemeci L, et al. The analgesic and sedative effects of intrathecal midazolam in perianal surgery. Eur J Anaesthesiol. 2004;21:658–62. http://dx.doi.org/10.1097/00003643-200408000-00012
25. Shadangi BK, Garg R, Pandey R, et al. Effects of intrathecal midazolam in spinal anaesthesia: a prospective randomised case control study.Singapore Med J. 2011;52:432–5
26. Talebi H, Yazdi B, Alizadeh S, et al. Effects of combination of intrathecal lidocaine and two doses of intrathecal midazolam on post-operative pain in patients undergoing herniorrhaphy: a randomized controlled trial. Pak J Biol Sci. 2010;13:1156–60.
27. Prakash S, Joshi N, Gogia AR, et al. Analgesic efficacy of two doses of intrathecal midazolam with bupivacaine in patients undergoing cesarean delivery. RegAnesth Pain Med. 2006;31:221–6. http://dx.doi. org/10.1097/00115550-200605000-00008
28. Chattopadhyay A, Maitra S, Sen S, et al. A study to compare the analgesic efficacy of intrathecal bupivacaine alone with intrathecal bupivacaine midazolam combination in patients undergoing elective infraumbilical surgery. Anesthesiol Res Pract. 2013; Article ID 567134:1–5. doi: 10.1155/2013/567134
29. Yegin A, Sanli S, Dosemeci L, et al. The analgesic and sedative effects of intrathecal midazolam in perianal surgery. Eur J Anaesthesiol. 2004;21:658–62. http://dx.doi.org/10.1097/00003643-200408000-00012,
30. Talebi H, Yazdi B, Alizadeh S, et al. Effects of combination of intrathecal lidocaine and two doses of intrathecal midazolam on post-operative pain in patients undergoing herniorrhaphy: a randomized controlled trial. Pak J Biol Sci. 2010;13:1156–60.
31. Maeda A, Katafuchi T, Oba Y, et al. Enhancement of GABAergic tonic currents by midazolam and noradrenaline in rat substantial gelatinosa neurons in vitro. Anesthesiology.2010;113:429–37. http://dx.doi.org/10.1097/ALN.0b013e3181e19bd4
32. Mendelson WB. Neuropharmacology of sleep induction by benzodiazepines. Crit Rev Neurobiol. 1992;6:221- 32, Strange PG. D1/D2 dopamine receptor interaction at the biochemical level. Trends Pharmacol Sci. 1991;12:48, Möhler H, Fritschy J, Rudolph U. A new benzodiazepine pharmacology. J PharmacolExpTher. 2002;300:2-8
33. Shadangi BK, Garg R, Pandey R, Das T. Effects of intrathecal midazolam in spinal anaesthesia: a prospective randomised case control study. Singapore Med J. 2011;52:432-5.
34. Chattopadhyay A, Maitra S, Sen S, Bhattacharjee S, Layek A, Pal S, et al. A study to compare the analgesic efficacy of intrathecal bupivacaine alone with intrathecal bupivacaine midazolam combination in patients undergoing elective infraumbilical surgery. Anesthesiol Res Pract. 2013;2013:567134.
35. Salimi A, Nejad RA, Safari F, Mohajaerani SA, Naghade RJ, Mottaghi K. Reduction in labor pain by intrathecal midazolam as an adjunct to sufentanil. Korean J Anesthesiol. 2014;66:204-9.
36. Walser A, Benjamin LE, Flynn T, Mason C, Schwartz R, Fryer RI. Quinazolines and 1, 4-benzodiazepines. 84. Synthesis and reactions of imidazo [1, 5-a][1, 4] benzodiazepines. J Org Chem. 1978;43:936-44, Reves JG, Fragen RJ, Vinik HR, Greenblatt DJ. Midazolam: pharmacology and uses. Anesthesiology. 1985;62:310-24.
37. Kim MH, Lee YM. Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy. 2001;86(1):77–9.
38. Y. K. Batra, K. Jain, P. Chari, M. S. Dhillon, B. Shaheen, and G.M. Reddy, "Addition of intrathecal midazolam to bupivacaine produces better post-operative analgesia without prolonging recovery," International Journal of Clinical Pharmacology and Therapeutics, vol. 37, no. 10, pp. 519–523, 1999.
39. M. H. Kim and Y. M. Lee, "Intrathecal midazolam increases the analgesic effects of spinal blockade with bupivacaine in patients undergoing haemorrhoidectomy," British Journal ofAnaesthesia, vol. 86, no. 1, pp. 77–79, 2001.
40. N. Bharti, R. Madan, P. R. Mohanty, andH. L. kaul, "Intrathecal midazolam added to bupivacaine improves the duration and quality of spinal anaesthesia," ActaAnaesthesiologicaScandinavica, vol. 47, no. 9, pp. 1101–1105, 2003.
41. Batra YK, Jain K, Chari P, Dhillon MS, Shaheen B, Reddy GM. Addition of intrathecal midazolam to bupivacaine produces better post-operative analgesia without prolonging recovery. Int J ClinPharmacolTher 1999; 37:519–523
42. Goodchild CS, Noble J. The effects of intrathecal midazolam on sympathetic nervous system refl exes in man — a pilot study. Br J ClinPharmacol 1987; 23:279–285
43. Prochazka J, Hejcl A, Prochazkova L. Intrathecal midazolam as supplementary analgesia for chronic lumbar pain-15 years' experience. Pain Med 2011;12:1309–1315
44. Tucker AP ,Mezzatesta J , Nadeson R , Goodchild CS. Intrathecal midazolam II: combination with intrathecal fentanyl for labor pain. AnesthAnalg 2004; 98:1521–1527
45. Tucker et al. assessed the analgesic effect and safety of intrathecal midazolam in

combination with fentanyl during labor.
46. A. Yegin, S. Sanli, L. Dosemeci, N. Kayacan, M. Akbas, and B. Karsli, "The analgesic and sedative effects of intrathecalmidazolamin perianal surgery," European Journal of Anaesthesiology, vol. 21, no. 8, pp. 658–662, 2004.
47. Chattopadhyay A, Maitra S, Sen S, Bhattacharjee S, Layek A, Pal S, et al. A Study to Compare the Analgesic Efficacy of Intrathecal Bupivacaine Alone with Intrathecal Bupivacaine Midazolam Combination in Patients Undergoing Elective Infraumbilical Surgery. 2013;2013.
48. J. G. Reves, R. J. Fragen,H.R.Vinik, andD. J. Greenblatt, "Midazolam: pharmacology and uses," Anesthesiology, vol. 62, no. 3, pp. 310–324, 1985.
49. Giovannitti JA. Midaolam: Versatle Agent for Use. 2014;(September).
50. Gerecke M: Chemical structure and properties of midazolam compared with other benzodiazepines. Br J ClinPharmacol 1983;16:11S-16S
51. Kupietzky A. Midazolam: a review of its use for conscious sedation of children. 1993;15(4):237–41.
52. Pagano RR, Graham CW, Galligan M, Conner JT, Katz RL: Histopathology of veins after intravenous lorazepam and RO 21-3981. Can AnaesthSoc J 1978;25:50-52.
53. Faull RLM, Villiger JW. Benzodiazepine receptors in the human spinal cord: a detailed anatomical and pharmacological study. Neuroscience 1986; 17: 791±802
54. Goodchild CS, Serrao JM. Intrathecal midazolam in the rat: evidence for spinally-mediated analgesia. Br J Anaesth 1987; 59:1563±70)
55. Hasan SKA. Effect of addition of intrathecal midazolam to 0 . 5 % hyperbaric bupivacaine to prolong the post-operative analgesia in lower abdominal surgeries. 2019;6(3):790–5.