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A Comparative Study of Intrathecal Magnesium Sulfate Versus Buprenorphine as Adjuvant To 0.5% Hyperbaric Bupivacaine In Patients Undergoing Infra Umbilical Surgeries Under Spinal Anaesthesia

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Abstract
Introduction: *Use of various adjuvants to spinal anesthesia is a well-known modality to provide intra-operative and post-operative analgesia. This study was designed to evaluate and compare the analgesic efficacy of buprenorphine and magnesium sulphate when used as an additive to intrathecal 0.5% hyperbaric bupivacaine.*
Materials and Methods: *135 patients of the American Society of Anaesthesiologist's physical status grade I or II, scheduled for lower abdominal surgery under spinal anaesthesia, were randomly allocated into three groups. Group B received 3 mL of 0.5% hyperbaric bupivacaine with 60mcg(0.2ml) of buprenorphine added to 0.3cc of normal saline, Group M received 3 mL of 0.5% hyperbaric bupivacaine with 75mg (0.15ml) magnesium sulfate 50% added to 0.35cc normal saline and Group C received 3 mL of 0.5% hyperbaric bupivacaine with 0.5ml of normal saline. Total volume being 3.5ml in all the groups. The primary outcome variable was duration of analgesia and secondary outcome variables included onset and duration of sensory and motor block. Data was analysed with chi-square test, Fischer's exact test and Mann Whitney U test.*
Results: *The time to first rescue analgesia was significantly ($P < 0.001$) longer in the Group B (412.78 ± 13.92 min) than both the Groups. Group M (302.44 ± 32.38 min) Showed significantly prolonged analgesia than Group C (217.00± 10.19min). Group B and Group M showed significantly prolonged duration of both sensory and motor block compared to Group C.*
Conclusion: *Intrathecal buprenorphine added to bupivacaine prolongs the duration of post-operative analgesia and prolongs the duration of sensory and motor block compared to magnesium sulfate and controls.*
Key Words: *Bupivacaine, Buprenorphine, Magnesium sulfate (sulphate), spinal anaesthesia.*

I. Introduction

Spinal anaesthesia is the most common technique of regional anaesthesia used for infra-umbilical surgeries. Local anaesthetic bupivacaine is the commonest agent used for spinal anaesthesia but its relatively shorter duration of action may lead to early analgesic intervention in post operative period.1

Opioids are commonly used as intrathecal adjuvants to improve the quality of intraoperative analgesia and prolong it in post operative period.

Buprenorphine is a centrally acting partial opioid agonist with both spinal and supraspinal component of analgesia2. It is highly lipid soluble and diffuses quickly into neural tissue, decreasing the chances of rostral spread leading to lesser side effects in the post operative period.3

Magnesium possesses a property of NMDA receptor antagonist. NMDA receptor antagonist plays an important role in the prevention of central sensitization of pain. Glutamate and aspartate neurotransmitters are released in response to noxious stimuli and bind to the NMDA receptors and various other excitatory amino acid receptors. NMDA receptors activation leads to calcium and sodium influx into the cell, efflux of potassium and initiation of central sensitization, and wind-up.4,5

This study was undertaken to compare magnesium sulfate and buprenorphine as adjuvant to hyperbaric bupivacaine in spinal anaesthesia.

II. Materials And Methods

Method of collection of data
Study design: Prospective Randomized double-blind study.
Study period: November2017–May2019.
Place of study: Inpatients at hospitals attached to Bangalore Medical College and Research Institute, Bangalore.

Sample size: Sample size was chosen based on previous study, time to mobilize with minimum difference of 1, 80% statistical power,5% level of significance, the sample sizeof45ineachgroupisadequateforthe study. We have chosen sample size of45ineachgroup.

Inclusion Criteria:

- Patients who are willing to give written informed consent
- Patients of age 18-60 years of either sex
- American society of anaesthesiologists (ASA)grade I and II.
- Patientswithheight150-180cmsandweight50-80kg.
- Patientsundergoingelective infraumbilicalsurgeries.

Exclusion Criteria:

- Patients not willing to give written informed consent
- Patients with any contraindications for neuraxial blockade
- Allergy to the study drug
- Coagulation disorders
- Cardiogenic or hypovolemic shock
- Respiratory insufficiency

Methodology: After obtaining clearance and approval from Institutional Ethical Committee, patients fulfilling inclusion criteria were willing to give written informed consent were included in the study and was randomly allocated in one of the three groups using numbers generated from www.random.org. The study drug was prepared by anaesthesiologist not involved in the study.

1. Group C (n= 45)- Bupivacaine (0.5%H) 3ml with 0.5ml normal saline.
2. Group M (n=45)-Bupivacaine(0.5%H) 3ml with 75mg(0.15ml) magnesium sulfate 50% added to 0.35cc normal saline
3. Group B (n=45)-Bupivacaine(0.5%) 3ml with 60mcg(0.2ml) buprenorphine added to 0.3cc of normal saline.

All patients were kept fasting for 8 hours. Tab Alprazolam 0.25mg and Tab Ranitidine 150mg was given night before the day of surgery. Inj. Ranitidine 50mg and Inj. Metoclopramide 10mg intravenously was given half an hour preoperatively. On arrival to the operating room, intravenous access was secured and patients are preloaded with 10ml/kg of Ringer lactate. Non Invasive Blood Pressure, Pulse oximetry and electrocardiogram was connected.
The baseline Systolic and Diastolic blood pressures (SBP, DBP), Heart Rate (HR) and\ Oxygen Saturation (SpO2) was recorded.
Under strict aseptic precautions Subarachnoid Block was performed using 25G/26 G Quincke Babcock spinal needle in the L3-L4 space with patient in left lateral position. The study drug was injected over 10-15 seconds. The time at which injection is completed was considered as zero time of the study and all measurements were Recorded from this point. Following Subarachnoid Block, patients was made to lie supine. Efficacy parameters were assessed as follows:

Sensory testing was assessed by loss of pinprick sensation to 23 G sterile hypodermic needle for onset and dermatome levels were tested until the highest level was achieved and stabilized for four consecutive tests.

Time of onset of Motor block wasassessed using Modified Bromage Scale .
Data regarding the time to reach highest dermatome level of sensory blockade from the time of injection, time for two segment sensory regression was collected.
In cases of failure of subarachnoid block and conversion to general anaesthesia, we excluded such patients from the study.
Haemodynamic variables was recorded every two minutes for first ten minutes, at 5 minutes for next 90 mins after the administration of subarachnoid block and every 15 minutes thereafter until the end of surgery. Postoperatively patient was monitored every 1hr for the first 4hours and then every 4 hours for 24 hours.
Hypotension is defined as 20% fall in Systolic Blood Pressure from baseline and was treated with intravenous fluids and intravenous Injection Mephentermine 6mg.
Bradycardia is defined as 20% fall in heart rate from baseline and was treated with intravenous Injection Atropine 0.6 mg.
After the surgery, patients were shifted to the post anesthesia care and recovery unit where they remained until complete recovery of sensory and motor blockade was achieved.

The incidence of any adverse effects such as hypotension, bradycardia, shivering, nausea, vomiting, pruritis, respiratory depression and ECG changes was recorded.
Time to gain back the motor function of lower limb, defined as time to reach modified Bromage 0 was noted.
Duration of sensory block was defined as the time taken for analgesia to regress till S2.
Duration of analgesia was defined as time taken from intrathecal drug administration to the time of first analgesic request.

Statistical analysis: Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22version software. Categorical data was represented in the form of Frequencies and proportions. Chi-square test was used as test of significance for qualitative data. Continuous data was represented as mean and standard deviation.
Independent t test was used as test of significance to identify the mean difference between two quantitative variables.

p value (Probability that the result is true) of <0.05 was considered as statistically significant after assuming all the rules of statistical tests.
Statistical software: MS Excel, SPSS version 22 (IBM SPSS Statistics, Somers NY, USA) was used to analyze data.
SAMPLE SIZE ESTIMATION: Sample size was chosen based on previous study, time to mobilize with minimum difference of 1, 80% statistical power,5% level of significance, the sample size of 45 in each group is adequate for the study. We chose sample size of 45 in each group.

III. Results

Table1:Age Distribution between three Groups

		Group							
		Buprenorphine		Magnesium		Control		Total	
		Count	%	Count	%	Count	%	Count	%
Age	≤30Years	2	4.44%	10	22.22%	11	24.44%	23	17.04%
	31-40 Years	18	40.00%	13	28.89%	19	42.22%	50	37.04%
	41-50 Years	21	46.67%	18	40.00%	13	28.89%	52	38.52%
	> 50Years	4	8.89%	4	8.89%	2	4.44%	10	7.41%
	Total	45	100.00%	45	100.00%	45	100.00%	135	100.00%

In Buprenorphine group, majority of subjects were in the age group 41 to 50 years(46.67%), in Magnesium group, majority of subjects were in the age group 41 - 50 Years(40%) and in control group, majority of subjects were in the group 31 - 40 Years(42.22%).Therewasnosignificantdifferenceinagedistributionbetweenthreegroups.

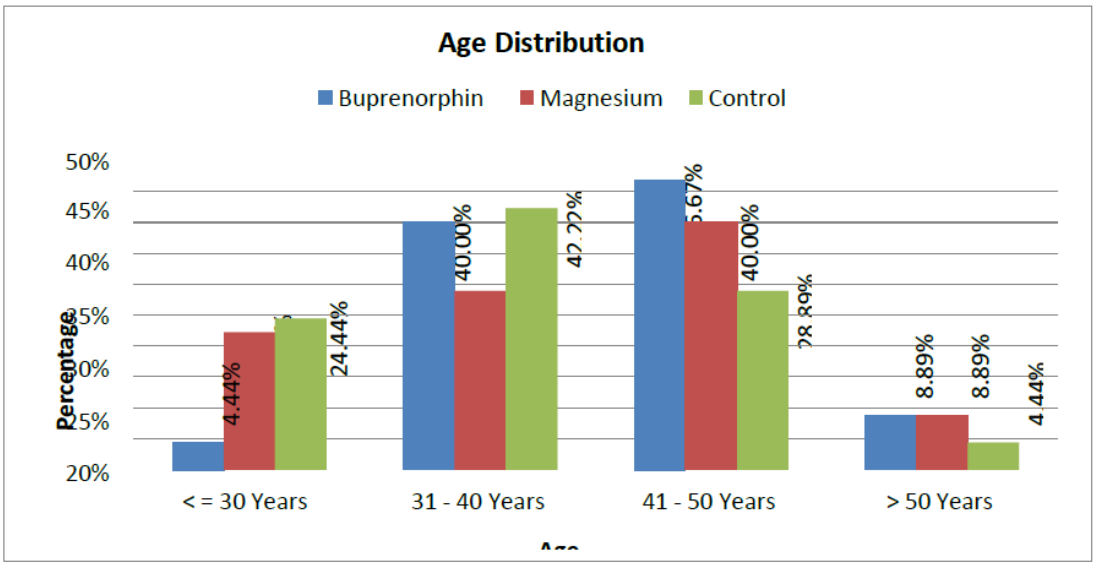

Figure 1 : Bar Diagram Showing Age Distribution between three Groups

Table2: Mean Age Comparison between three Groups

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Age	41.11	7.12	39.36	10.08	37.27	8.46	39.24	8.72	0.111

Mean age in Buprenorphine group was 41.11 ± 7.12 years, in Magnesium group was 39.36 ± 10.08 years and in Control group was 37.27 ± 8.46 years. There was no significant difference in age distribution between three groups.

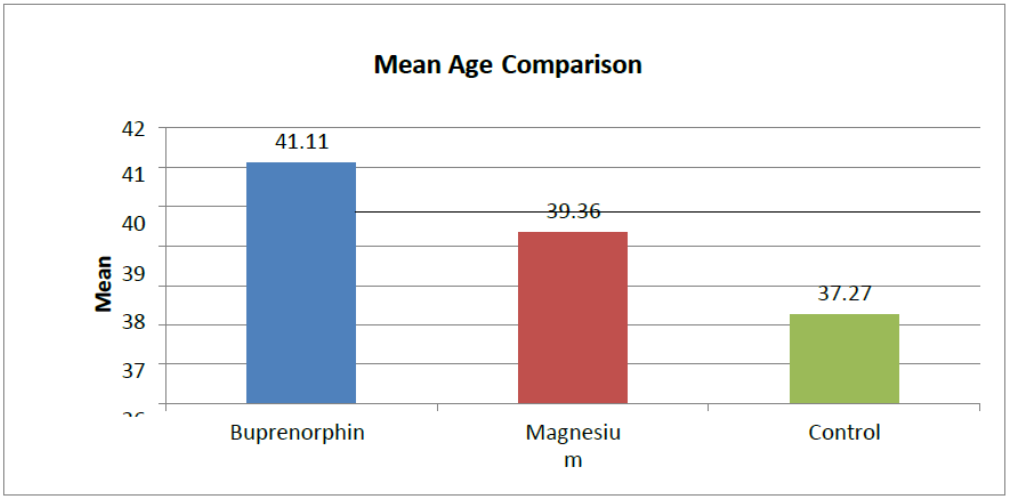

Figure 2 : Bar Diagram Showing Mean Age Comparison between three Groups

Table3: Sex Distribution between three groups

		Group							
		Buprenorphine		Magnesium		Control		Total	
		Count	%	Count	%	Count	%	Count	%
Sex	Female	22	48.89%	23	51.11%	17	37.78%	62	45.93%
	Male	23	51.11%	22	48.89%	28	62.22%	73	54.07%
	Total	45	100.00%	45	100.00%	45	100.00%	135	100.00%

χ 2=1.849,df=2,p=0.397

In Buprenorphine group, 48.89% were females and 51.11% were males, in Magnesium group, 51.11% were females and 48.89% were males and in control group, 37.78% were females and 62.22% were males. There was no significant difference in sex distribution between three groups.

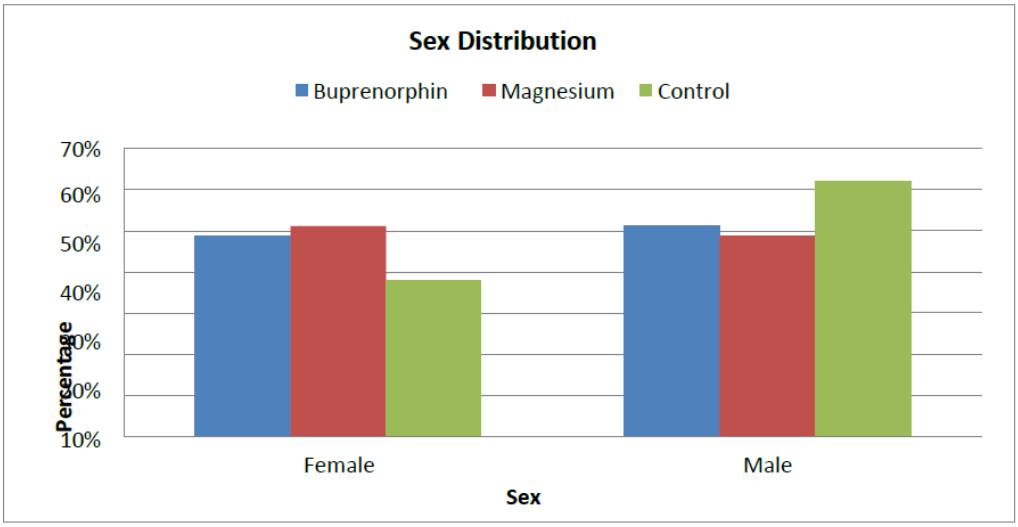

Figure 3: Sex Distribution between three groups

Table4: Mean Weight, Height and BMI Distribution between three groups

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Weight (Kg)	62.71	8.18	59.82	5.63	61.38	6.17	61.30	6.81	0.131
Height(Mts)	1.60	0.05	1.59	0.05	1.58	0.05	1.59	.05	0.295
BMI	24.54	2.59	23.81	2.61	24.61	2.59	24.32	2.60	0.272

In Buprenorphine group, mean weight was 62.71 ± 8.18 kgs, mean height was 1.60 ± 0.05 mts, mean BMI was 24.54 ± 2.59. In Magnesium group, mean weight was 59.82 ± 5.63 kgs, mean height was 1.59 ± 0.05 mts, mean BMI was 1.58 ± 0.05. There was no significant difference in mean weight, height and BMI between three groups.

Table5: ASA Distribution between three groups

		Group							
		Buprenorphine		Magnesium		Control		Total	
		Count	%	Count	%	Count	%	Count	%
ASA	1	30	66.67%	35	77.78%	28	62.22%	93	68.89%
	2	15	33.33%	10	22.22%	17	37.78%	42	31.11%

χ 2=2.696,df=2,p=0.260

In Buprenorphine group, 66.67% had ASA grade 1 and 33.3% had ASA grade 2. In Magnesium group, 77.78% had ASA grade 1 and 22.22% had ASA grade 2 and in Control group, 62.22% had ASA grade 1 and 37.78% had ASA grade 2. There was no significant difference in ASA grade between three groups.

Table 6: Mean Duration of Surgery, Onset of Sensory Block at T10 and Onset of Sensory Block at highest level Comparison between three groups

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Duration O fSurgery	68.09	25.80	82.64	13.35	73.33	13.31	74.69	19.28	0.001*

Onset Of SensoryBlock AtT10 (Minutes)	3.83	0.45	6.70	0.37	3.82	0.45	4.79	1.42	<0.001*
Onset Of SensoryBlock At HighestSensoryLevel (Minutes)	5.85	0.32	9.58	0.58	5.84	0.33	7.09	1.82	<0.001*

In Buprenorphine group, mean Duration of Surgery was 68.09 ± 25.80 min, mean Onset Of Sensory Block At T10 was 3.83 ± 0.45 min and mean Onset Of Sensory Block At Highest Sensory Level was 5.85 ± 0.32 min. In Magnesium group, mean Duration of Surgery was 82.64 ± 13.35 min, mean Onset of Sensory Block at T10 was 6.70 ± 0.37 min and mean Onset of Sensory Block at Highest Sensory Level was 9.58 ± 0.58 min. In Control group, mean Duration of Surgery was 73.33 ± 13.31 min, mean Onset of Sensory Block at T10 was 3.82 ± 0.45 min and mean Onset of Sensory Block at Highest Sensory Level was 5.84 ± 0.33 min. There was significant difference in mean Duration of Surgery, Onset of Sensory Block at T10 and Onset of Sensory Block at Highest Sensory Level between three groups.

Table7: Max Height of Sensory Block Distribution between three groups

		Group							
		Buprenorphine		Magnesium		Control		Total	
		Count	%	Count	%	Count	%	Count	%
Max Height ofSensoryBlock	T4	1	2.22%	0	0.00%	1	2.22%	2	1.48%
	T6	19	42.22%	20	44.44%	20	44.44%	59	43.70%
	T7	9	20.00%	8	17.78%	7	15.56%	24	17.78%
	T8	16	35.56%	17	37.78%	17	37.78%	50	37.04%

χ 2=1.324,df=6,p=0.970

In Buprenorphine group, majority of subjects had Max Height Of Sensory Block at T6 (42.22%), in magnesium group, majority of subjects had Max Height Of Sensory Block at T6 (44.44%) and in Cotnrol group, majority of subjects had Max Height Of Sensory Block at T6 (44.44%). There was no significant difference in Max Height Of Sensory Block between three groups.

Table 8: Mean 2 dermatome sensory block regression time (minute), total duration of sensory block (minute), onset of motor block (minutes), duration of motor block (minutes) and time for first analgesic dose (minutes) comparison between three groups

	Group								Pvalue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
2 Dermatome Sensory Block Regression Time(minute)	142.51	5.23	132.24	4.65	119.89	5.34	131.55	10.56	<0.001*
Total Duration Of Sensory Block (minute)	285.20	7.00	222.42	6.45	181.78	8.27	229.80	43.31	<0.001*
Onset Of Motor Block(minutes)	4.67	0.35	7.98	0.37	4.80	0.35	5.82	1.58	<0.001*
Duration Of Motor Block(minutes)	260.11	7.66	201.58	8.41	166.22	8.67	209.30	39.72	<0.001*
Time For First Analgesic Dose (minutes)	412.78	13.92	302.44	32.38	217.00	10.19	310.74	83.14	<0.001*

In Buprenorphine group, mean 2 Dermatome Sensory Block Regression Time was
142.51 ± 5.23 min, mean Total Duration of Sensory Block was 285.20 ± 7.00 min, mean Onset of Motor Block was 4.67 ± 0.35 min, mean Duration of Motor Block was 260.11
± 7.66 min and mean Time for First Analgesic Dose was 412.78 ± 13.92 min. In Magnesium group, mean 2 Dermatome Sensory Block Regression Time was 132.24 ±
4.65 min, mean Total Duration of Sensory Block was 222.42 ± 6.45 min, mean Onset of Motor Block was 7.98 ± 0.37 min, mean Duration of Motor Block was 201.58 ± 8.41 min and mean Time For First Analgesic Dose was 302.44 ± 32.38 min. In Control group, mean 2 Dermatome Sensory Block Regression Time was 119.89 ± 5.34 min, mean Total Duration of Sensory Block was 181.78 ± 8.27 min, mean Onset of Motor Block was
4.80 ± 0.35 min, mean Duration of Motor Block was 166.22 ± 8.67 min and mean Time for First Analgesic

Dose was 217.00 ± 10.19 min. There was significant difference in 2
dermatome Sensory Block Regression Time, Total Duration of Sensory Block, Onset Of Motor Block, Duration Of Motor Block and Time For First Analgesic Dose between three groups.

Table9: Mean Pulse Comparison between three groups at different time intervals

	Group								Pvalue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Baseline	83.18	8.28	83.58	9.02	90.84	12.23	85.87	10.53	<0.001*
2min	83.13	7.23	82.51	8.67	83.13	7.23	82.93	7.69	0.908
4min	79.69	7.08	80.56	7.87	79.69	7.08	79.98	7.31	0.812
6min	77.42	7.23	79.31	7.98	77.42	7.23	78.05	7.49	0.388
8min	75.87	6.84	78.82	8.69	75.87	6.84	76.85	7.58	0.102
10min	73.71	6.74	77.38	8.20	73.71	6.74	74.93	7.41	0.024*
15min	72.53	6.91	76.27	8.80	72.53	6.91	73.78	7.74	0.029*
20min	72.09	6.99	75.87	9.58	72.09	6.99	73.35	8.09	0.037*
25min	71.67	8.11	75.98	9.27	71.67	8.11	73.10	8.69	0.024*
30min	71.44	7.01	76.78	9.16	71.44	7.01	73.22	8.14	0.001*
35min	71.77	7.23	76.31	9.22	71.56	7.30	73.22	8.22	0.007*
40min	71.37	7.41	75.00	7.40	71.58	7.50	72.67	7.57	0.038*
45min	70.89	8.10	75.77	6.76	71.84	7.38	72.98	7.62	0.008*
50min	71.29	8.95	74.39	7.82	71.81	8.04	72.64	8.25	0.200
55min	70.10	6.48	75.65	8.35	71.10	6.34	72.55	7.55	0.002*
60min	70.69	7.48	75.35	7.73	71.83	6.97	72.94	7.59	0.022*
75min	70.36	7.08	74.61	7.72	72.37	7.29	72.87	7.55	0.092
90min	71.47	8.31	74.06	7.08	75.53	8.61	73.82	7.88	0.300
105min	72.38	7.73	76.82	7.41	80.00	.	75.20	7.55	0.383
120min	72.00	8.00	.	.	.	.	72.00	8.00	
Imm.Postop	71.29	8.98	70.98	7.26	67.80	2.75	70.02	6.98	0.031
1hr	71.64	9.43	71.51	5.91	69.62	2.81	70.93	6.64	0.273
2hr	74.44	6.49	73.56	6.28	72.38	2.94	73.46	5.51	0.204
3hr	73.82	6.41	75.18	6.18	73.56	3.15	74.19	5.46	0.321
4hr	76.16	4.72	77.64	6.45	76.62	3.00	76.81	4.93	0.345
8hr	78.98	5.73	79.27	6.91	80.09	4.18	79.44	5.69	0.634
12hr	77.49	6.10	80.18	6.95	80.71	5.96	79.46	6.46	0.039*
16hr	80.71	6.59	81.22	8.69	82.96	6.03	81.63	7.21	0.304
20hr	82.33	6.39	82.47	9.23	84.49	6.48	83.10	7.49	0.313
24hr	82.56	6.97	83.71	9.19	85.56	6.91	83.94	7.80	0.185

In the study there was significant difference in mean PR at baseline, from 10 min to 45 min, 55 min, 60 min and 12 hr post op between three groups. At other intervals there was no significant difference in mean PR between three groups at other intervals.

Table 10: Mean SBP Comparison between three groups at different time intervals

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
SBP	133.13	10.53	131.98	10.62	127.18	10.57	130.76	10.81	0.606
2min	117.11	13.29	117.20	11.06	115.53	8.56	116.61	11.08	0.973
4min	113.82	8.89	113.38	9.01	112.67	8.33	113.29	8.70	0.814
6min	112.80	7.88	112.73	9.24	109.67	7.38	111.73	8.27	0.971
8min	111.44	6.76	113.04	7.51	108.91	5.90	111.13	6.92	0.291
10min	110.89	4.69	111.60	5.36	109.78	6.34	110.76	5.52	0.505
15min	108.49	5.85	110.62	6.45	109.40	6.93	109.50	6.44	0.104
20min	109.64	8.15	110.53	7.98	109.02	6.37	109.73	7.51	0.602
25min	110.62	7.06	111.02	7.27	107.89	9.03	109.84	7.90	0.792
30min	109.51	7.93	109.42	8.58	108.00	8.26	108.98	8.23	0.959
35min	109.05	7.56	109.20	7.39	109.62	9.83	109.29	8.28	0.923
40min	107.98	10.46	109.89	12.13	110.07	11.37	109.33	11.31	0.431
45min	108.03	10.75	105.50	9.13	110.18	11.53	107.89	10.60	0.262
50min	108.29	12.03	106.98	11.04	111.47	10.76	108.96	11.28	0.626
55min	108.31	11.53	107.42	10.45	111.49	8.98	109.12	10.31	0.734
60min	109.62	11.42	108.30	8.91	109.93	17.78	109.22	13.31	0.596
75min	108.36	9.74	109.88	7.72	110.84	8.57	109.85	8.46	0.501
90min	107.39	7.87	111.25	7.88	109.00	9.78	109.62	8.47	0.103
105min	111.88	10.60	111.82	7.81	108.00	.	111.65	8.62	0.989
120min	110.80	12.64	.	.	.	.	110.80	12.64	-
ImmPostop	119.69	11.77	113.69	13.76	118.16	13.20	117.18	13.09	0.029*
1hr	122.58	9.73	118.33	9.32	120.53	10.88	120.48	10.08	0.037*
2hr	124.84	9.16	121.13	8.38	121.84	10.24	122.61	9.36	0.048*
3hr	125.11	11.42	122.62	8.36	121.56	12.21	123.10	10.82	0.241
4hr	125.91	11.18	123.91	10.49	121.09	11.45	123.64	11.14	0.384
8hr	126.24	11.51	124.00	9.89	122.49	11.26	124.24	10.94	0.324
12hr	125.11	12.62	121.58	8.67	120.42	11.95	122.37	11.31	0.125
16hr	123.44	13.07	123.09	10.36	121.24	11.04	122.59	11.50	0.887
20hr	125.36	11.62	124.80	8.96	123.84	10.94	124.67	10.51	0.800
24hr	127.98	10.62	128.49	9.20	128.40	8.28	128.29	9.35	0.808

In the study there was significant difference in mean SBP at immediate post op, 1 hr and 2 hr. At other intervals there was no significant difference in mean SBP between three groups.

Table 11 : Mean DBP Comparison between three groups at different time intervals

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
DBP	75.51	10.15	76.71	8.44	81.91	6.93	78.04	8.99	0.544

2min	65.82	7.60	65.16	6.42	62.20	6.70	64.39	7.05	0.654
4min	65.93	4.68	65.82	5.56	65.93	5.33	65.90	5.17	0.919
6min	64.96	4.89	65.02	5.22	67.51	5.87	65.83	5.44	0.950
8min	64.16	4.26	64.51	5.17	67.42	6.22	65.36	5.44	0.723
10min	63.96	4.23	64.22	4.37	67.13	6.20	65.10	5.18	0.770
15min	64.62	4.51	64.96	5.24	69.71	6.38	66.43	5.87	0.747
20min	64.98	4.49	66.16	4.39	69.69	5.27	66.94	5.11	0.212
25min	64.29	3.82	65.04	4.25	72.07	7.08	67.13	6.29	0.378
30min	64.38	4.38	65.07	4.91	74.04	7.48	67.83	7.22	0.484
35min	64.20	3.78	65.29	4.22	79.47	9.72	69.69	9.52	0.205
40min	63.42	5.38	64.67	3.66	70.42	6.90	66.21	6.24	0.205
45min	64.74	5.07	63.75	4.81	71.77	7.85	66.90	7.11	0.376
50min	63.84	3.87	65.09	5.88	70.88	7.48	66.87	6.80	0.303
55min	64.24	4.09	64.98	5.05	72.71	7.17	67.59	6.87	0.516
60min	64.27	3.90	64.49	4.74	71.07	5.49	66.89	5.81	0.843
75min	64.55	4.67	64.56	3.58	74.06	7.98	67.76	7.19	0.988
90min	63.94	3.52	65.13	3.44	75.00	9.02	67.54	7.20	0.254
105min	63.88	3.27	67.09	2.81	92.00	.	67.05	6.72	0.034*
120min	63.80	2.77	.	.	.	.	63.80	2.77	
Imm.Postop	65.58	8.56	62.20	6.70	62.87	7.28	63.55	7.64	0.040*
1hr	68.16	6.18	65.93	5.33	66.04	5.49	66.71	5.73	0.071
2hr	69.29	6.06	67.51	5.87	66.78	4.94	67.86	5.70	0.161
3hr	69.04	8.51	67.42	6.22	66.24	4.80	67.57	6.74	0.305
4hr	67.78	8.12	67.13	6.20	65.56	4.87	66.82	6.55	0.673
8hr	67.49	8.85	69.71	6.38	66.76	5.48	67.99	7.11	0.175
12hr	68.93	8.13	69.69	5.27	68.33	5.29	68.99	6.35	0.602
16hr	69.18	7.40	72.07	7.08	69.78	7.08	70.34	7.24	0.062
20hr	69.71	7.62	74.49	8.63	72.60	9.25	72.27	8.69	0.007*
24hr	69.93	7.35	79.91	10.19	78.27	11.52	76.04	10.71	<0.001*

In the study there was significant difference in mean DBP between three groups at 105min, immediate post op, 20 hr and 24 hr. At other intervals there was no significant difference in mean DBP between three groups.

Table 12: Mean MAP Comparison between three groups at different time intervals

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
MAP	94.69	8.96	95.09	8.03	96.51	8.27	95.43	8.40	0.824
2min	82.98	8.44	82.51	6.15	79.98	5.29	81.82	6.83	0.765
4min	81.93	4.89	81.60	4.61	81.53	4.51	81.69	4.64	0.740
6min	80.93	4.84	81.00	4.61	81.58	4.67	81.17	4.68	0.947
8min	79.89	4.09	80.69	4.52	81.20	4.42	80.59	4.35	0.381
10min	79.64	3.41	79.98	3.40	81.42	4.50	80.35	3.86	0.644

15min	79.27	3.90	80.18	4.15	82.91	4.71	80.79	4.51	0.286
20min	79.84	4.61	80.93	3.63	82.82	4.33	81.20	4.36	0.216
25min	79.73	3.54	80.38	3.49	84.04	5.17	81.39	4.53	0.387
30min	79.40	3.60	79.84	4.11	85.42	5.59	81.56	5.25	0.586
35min	79.14	3.38	79.91	3.83	89.51	7.80	82.88	7.15	0.315
40min	78.28	4.77	79.80	4.36	83.60	6.07	80.59	5.56	0.122
45min	79.20	5.11	77.64	4.35	84.55	7.27	80.55	6.48	0.146
50min	78.58	4.51	79.07	5.03	84.47	6.67	80.91	6.15	0.668
55min	78.90	4.97	79.19	5.31	85.61	5.89	81.44	6.26	0.817
60min	79.50	5.16	79.05	4.74	84.00	7.80	81.00	6.52	0.711
75min	79.09	4.29	79.63	3.85	86.41	6.71	81.79	6.02	0.610
90min	78.50	3.73	80.53	4.04	86.37	7.30	81.61	5.87	0.086
105min	79.88	4.26	81.91	4.16	97.00	.	81.85	5.43	0.312
120min	79.60	5.68	.	.	.	.	79.60	5.68	
Imm.Postop	83.58	8.02	79.38	7.75	81.29	4.57	81.41	7.12	0.013*
1hr	86.24	5.63	83.42	5.05	84.20	4.41	84.62	5.16	0.014*
2hr	87.80	5.26	85.40	4.71	85.13	4.41	86.11	4.92	0.025*
3hr	87.73	8.38	85.84	5.28	84.69	5.06	86.09	6.50	0.204
4hr	87.07	7.89	86.00	5.82	84.13	5.09	85.73	6.44	0.467
8hr	87.09	8.53	87.78	5.69	85.36	5.30	86.74	6.69	0.653
12hr	87.67	8.42	86.98	4.57	85.62	5.84	86.76	6.48	0.631
16hr	87.36	8.11	89.09	5.44	86.98	6.10	87.81	6.66	0.237
20hr	88.24	7.43	91.29	6.24	89.71	7.67	89.75	7.20	0.038*
24hr	89.22	7.17	96.02	8.16	95.00	7.83	93.41	8.24	<0.001*

In the study there was significant difference in mean MAP between three groups at immediate post op, 1 hr, 2 hr, 20 hr and 24 hr. At other intervals there was no significant difference in mean MAP between three groups.

Table 13: Mean RR Comparison between three groups at different time intervals

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Baseline	15.36	1.32	14.36	1.63	14.64	1.51	14.79	1.54	0.006*
Intraop	15.38	1.40	14.00	1.31	15.38	1.40	14.92	1.51	<0.001*
POST OPRR	13.80	1.27	13.36	1.17	13.80	1.27	13.65	1.25	0.149

In the study there was significant difference in mean RR at baseline, intra op and post op between three groups. Mean RR was high in Buprenorphine group compared to other groups.

Table 14: Mean SPO2 Comparison between three groups at different time intervals

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
SPO2	99.69	.60	99.69	.63	100.00	.00	99.79	.52	0.004*

2min	99.71	.55	99.91	.29	99.71	.55	99.78	.48	0.076
4min	99.73	.54	99.84	.37	99.73	.54	99.77	.49	0.462
6min	99.76	.61	99.91	.29	99.76	.61	99.81	.53	0.270
8min	99.53	.97	99.82	.53	99.53	.97	99.63	.85	0.180
10min	99.58	.89	99.76	.65	99.58	.89	99.64	.82	0.494
15min	99.56	.89	99.78	.56	99.56	.89	99.63	.80	0.315
20min	99.76	.65	99.96	.21	99.76	.65	99.82	.54	0.132
25min	99.89	.44	100.00	.00	99.89	.44	99.93	.36	0.239
30min	99.78	.52	99.87	.40	99.78	.52	99.81	.48	0.602
35min	99.73	.72	99.80	.59	99.73	.72	99.76	.67	0.865
40min	99.69	.70	99.84	.42	99.69	.70	99.74	.62	0.395
45min	99.76	.61	99.91	.29	99.76	.61	99.81	.53	0.270
50min	99.71	.76	99.82	.58	99.71	.76	99.75	.70	0.688
55min	99.87	.40	99.93	.25	99.87	.40	99.89	.36	0.601
60min	99.62	.86	99.84	.56	99.62	.86	99.70	.78	0.294
75min	99.73	.62	99.91	.29	99.73	.62	99.79	.53	0.190
90min	99.82	.39	99.87	.34	99.82	.39	99.84	.37	0.808
105min	99.73	.65	99.87	.40	99.73	.65	99.78	.58	0.458
120min	99.67	.67	99.80	.46	99.67	.67	99.71	.61	0.491
Imm.Postop	99.87	.46	99.78	.77	99.87	.46	99.84	.58	0.702
1hr	99.87	.40	99.84	.42	99.87	.40	99.86	.41	0.957
2hr	99.82	.44	99.91	.29	99.82	.44	99.85	.40	0.473
3hr	99.84	.42	99.82	.49	99.84	.42	99.84	.44	0.964
4hr	99.87	.40	99.87	.34	99.87	.40	99.87	.38	1.000
8hr	99.73	.54	99.76	.53	99.73	.54	99.74	.53	0.975
12hr	99.69	.60	99.69	.60	99.69	.60	99.69	.60	1.000
16hr	99.69	.60	99.69	.60	99.69	.60	99.69	.60	1.000
20hr	99.69	.60	99.69	.67	99.69	.60	99.69	.62	1.000
24hr	99.60	.75	99.64	.71	99.60	.75	99.61	.73	0.947

In the study there was significant difference inmean SpO2 between three groups at baseline. At other intervals there was no significant difference in mean SpO2 between three groups.

Table 15: Mean VAS Comparison between three groups at different time intervals

	Group								PValue
	Buprenorphine		Magnesium		Control		Total		
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	
Immediate PostOperative	0.00	0.00	0.00	0.00	0.00	0.00	0.00	0.00	-
1hr	0.00	0.00	1.42	0.92	0.00	0.00	0.47	0.85	<0.001*
2hr	0.93	1.01	1.78	0.64	0.93	1.01	1.21	0.98	<0.001*
6hr	6.20	0.73	6.49	0.51	6.00	0.90	6.23	0.75	0.007*
12hr	5.73	0.84	5.40	0.58	6.22	0.74	5.79	0.80	<0.001*
24hr	5.64	0.91	5.24	0.53	5.64	0.91	5.51	0.82	0.027*

In the study there was significant difference in mean VAS score from 1 hr to 24 hrpostop period between three groups. Mean VAS was high in Magnesium group till 6 hr andhighincontrolgroupfrom6hrto24hrs.

IV. Discussion

Spinal anaesthesia is the most preferred regional anaesthesia technique as it is easy to perform, produces rapid onset of anaesthesia and complete muscle relaxation and is also economical. These advantages are sometimes offset by a relatively short duration of action.

The aim of intrathecal local anesthetic is to provide adequate sensory and motor block necessary for all infra umbilical surgeries. Hyperbaric bupivacaine is the most commonly used intrathecal local anesthetic. Various adjuvants have been added to bupivacaine to prolong the duration of block.

Buprenorphine is a centrally acting partial opioid agonist with both spinal and supraspinal component of analgesia2. It is highly lipid soluble and diffuses quickly into neural tissue, decreasing the chances of rostral spread leading to lesser side effects in the post operative period.

Magnesium sulfate possesses a property of NMDA receptor antagonist. NMDA receptor antagonist plays an important role in the prevention of central sensitization of pain. Glutamate and aspartate neurotransmitters are released in response to noxious stimuli and bind to the NMDA receptors and various other excitatory amino acid receptors. NMDA receptors activation leads to calcium and sodium influx into the cell, efflux of potassium and initiation of central sensitization, and wind-up.

This prospective study was conducted to compare the analgesic effects of intrathecal magnesium sulfate and intrathecal buprenorphine in patients undergoing infra- umbilical surgeries. The patients were selected at random, to avoid any kind of bias and to allow comparability of results obtained. This was a double blind study where neither the patient nor the observer who recorded the parameters were aware of the group allocation and the drug received.

Dose fixation

In a study conducted by Jabalameli et al on different doses of intrathecal magnesium sulphate, found that 75mg of magnesium sulphate was enough for prolonged duration of sensory and motor blockade without any significant side effects. Hence we chose a dose of 75mg of magnesium sulphate for our study.

Singh AP et al in their study found that 60mcg of intrathecal buprenorphine prolonged the duration of sensory block and also prolongs the post operative pain relief. Duration of analgesia in this study was 7.44±1.69 hrs.6

In a study conducted by Koushic A Theerth et al, they found that 150mcg of buprenorphine when used intrathecally, prolonged the duration of analgesia which was 493.33±82.85 mins.
On comparing both the studies, we chose a dose of 60mcg of buprenorphine.

Patient characteristics across the groups

The mean age, weight and height of the patients in our study, in group B was 41.11±7.12 yrs, 62.71±8.18 kgs and 1.60±0.05 mts respectively and in group C was 37.27±8.46 yrs, 61.38±6.17 kgs and 1.58±0.05 mts respectively.
No statistically significant difference was noted between three groups. These parameters were kept identical in all groups to avoid variation in intra operative and post operative outcome of the patients.

Sensory block characteristics

Onset of sensory block: In our study the mean onset time of sensory block at highest level had significantdifference in all three groups with 5.85±0.32 mins for patients belonging to group B,9.58±0.58 mins for patients belonging to group M and 5.84±0.33 mins for patients belonging to group C. Mean onsettime of sensory block was delayed in magnesium group compared to other two groups.

Maximum height of sensory block: In our study, majority of the patients had maximum height of sensory block at T6 level with 42.22% of patients in group B, 44.44% in group M and 44.44% in group C. There was no significant difference in maximum height of sensory block achieved between three groups.
Two dermatome sensory block regression: The mean two dermatome sensory block regression time was 142.51±5.23 mins in group B, 132.24±4.65 mins in group M and 119.89±5.34 mins in group C which was statistically significant.

Duration of sensory block

There was statistically significant difference in total duration of sensory block with 285.20±7.00 mins in patients belonging to group B, 222.42±6.45 mins in patients belonging to group M and 181.78±8.27 mins in patients belonging to group C.

In Khandelwal et al study on comparison of intrathecal clonidine and magnesium, they found that magnesium prolongs the mean duration of sensory block but delays the onset of sensory block which is similar to our study.7

The results obtained by us were supported by Singh AP et al, whose study on effects of intrathecal buprenorphine on duration of spinal anaesthesia and found that addition of 60mcg of buprenorphine prolonged the duration of sensory block.

Our results were similar to Shukla et al study on comparison of intrathecal magnesium versus intrathecal dexmedetomidine as adjuvants to bupivacaine which showed delay in onset of sensory block and also prolonged mean duration of sensory block in magnesium group as compared to the control group.

Motor block characteristics

Onset of motor block

The mean time taken for onset of motor block in group B was 4.67±0.35 mins and in group M was 7.98±0.37 mins compared to 4.80±0.35 mins in group C which was statistically highly significant ($p<0.001$).

This shows that mean time of onset of motor block was delayed in group M as compared to group B and group C.

Duration of motor block

The mean duration of motor blockade in group B was 260.11±7.66 mins compared to 201.58±8.41 mins in group M and 166.22±8.67 mins in group C which was statistically highly significant.

This shows that addition of both buprenorphine and magnesium potentiates the motor blockade provided by bupivacaine when compared with control group.

In a study by Koushic A Theerth et al, the mean time of complete motor block was 7.06 mins in the magnesium group, 4.53 mins in buprenorphine group and 4.52 mins in the distilled water group. They concluded that the mean time of onset of complete motor block was significantly delayed in the magnesium group compared to the buprenorphine and distilled water groups which is similar to our study.8

Binesh kathuria et al in their study concluded that 75mg of magnesium delays the onset of motor block and prolongs the duration of motor block compared to the control group which also supports the results in our study.

Duration of analgesia: In our study the mean duration of analgesia was 412.78±13.92 mins in group B, 302.44±32.38 mins in group M and 217±10.19 mins in group C which was statistically significant.

The mean duration of analgesia is significantly more in group B and group M as compared to group C.

In Koushic A Theerth et al study, addition of buprenorphine and magnesium prolonged the duration of analgesia compared to control group which is similar to our study.

Binesh Kathuria et al in their study showed the addition of 75mg of magnesium to bupivacaine in spinal anaesthesia prolonged the mean duration of analgesia as compared to plain bupivacaine which is in accordance to our study.[9]

Hemodynamic parameters and VAS score

There was significant difference in mean pulse rate at baseline, from 10 min to 45 mins, 55 mins, 60 mins and 12 hr post op between three groups in our study.

At other intervals there was no significant difference in mean pulse rate between three groups.

Even though there was statistical significance in mean pulse rate at few time intervals, there was no significant changes in the pulse rate between three groups. There was no incidence of bradycardia in three groups. Pulse rate in three groups was within normal limits.

Mean SBP, DBP and MAP were comparable during the intra operative period between all the three groups.

In our study there was significant statistical difference in the mean VAS score from 1 hr to 24 hr post op period between three groups.

Mean VAS score was high in magnesium group till 6 hrs and high in control group from 6 hr to 24 hrs.

Mamta Khandelwal et al in their study found that heart rate was significantly ($p<0.05$) different among three groups from 5 mins to 50 mins which supports our study.

They also found that VAS score was significantly higher in control group compared to magnesium group, which is similar to our sudy.

Binesh Kathuria et al in their study on comparing two different doses of intrathecal magnesium found no difference in the mean blood pressure and mean VAS score was significantly high in control group as compared to magnesium group. These results are similar to the results obtained in our study.

Side effects: Opioids are associated with many side effects such as respiratory depression, nausea and vomiting, pruritis, urinary retention and hemodynamic instability.
In studies conducted by Gupta et al, Khandelwal et al, there was no significant adverse effects seen. In our study, no significant side effects were observed.[10]

V. Conclusion

We conclude that the addition of magnesium sulfate to bupivacaine in spinal anaesthesia delayed the time of onset of both sensory and motor block when compared to buprenorphine. The duration of sensory block, motor block and duration of analgesia was significantly prolonged in buprenorphine group when compared to magnesium sulfate group and control group. However, the duration of sensory block, motor block and duration of analgesia was significantly prolonged in magnesium sulfate group when compared to control group. There was good hemodynamic stability and without any significant side effects.

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