Original Research Article

A comparative study of magnesium sulphate v/s clonidine as adjuvants to intrathecal hyperbaric bupivacaine under spinal anaesthesia for infraumbilical surgeries

Vandana Hebballi[1], Navya SA[2], Anusha K M[3], Champa B V[4], Vishwanath V.M[5*]

[1]Senior Resident, Department of Anaesthesia, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India

[2]Senior Resident, Department of Anaesthesia, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India

[3]Intern, JSS Academy of Higher Education and Research, Mysuru, India

[4]Associate Professor, Department of Anesthesiology, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India

[5]Senior Resident, Department of Anaesthesia, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India

Received: 14-07-2021 / Revised: 10-08-2021 / Accepted: 22-09-2021

Abstract

Introduction: Spinal anaesthesia is the most common technique of regional anaesthesia used for lower abdominal and lower limb surgeries. Local anaesthetic Bupivacaine is the commonly administered drug. Many adjuvants to local anaesthetic have been used for intraoperative as well as post-operative period. In this study magnesium sulphate and alfa 2 adrenergic agonist Clonidine are used as adjuvant to hyperbaric bupivacaine. In this study we evaluate and compare the characteristics of spinal block and side effects in patients undergoing infraumbilical surgeries who received a subarachnoid block with either bupivacaine with magnesium sulphate or with clonidine. **Methods:** 90 patients of ASA I/II physical status undergoing elective infraumbilical surgeries were randomised into 2 groups. Group M (n=45) patients received 2.5ml of 0.5%bupivacaine with 30mg magnesium sulphate and Group C (n=45) patients received 2.5ml of 0.5% bupivacaine with 30mcg Clonidine. In both group, final drug volume made equal to 3ml by adding normal saline. Quality of block in terms of Time of Onset and total Duration of Sensory and Motor Blockade, 2 Segment regression time, Total analgesia time, Hemodynamic parameters and any Side Effects were recorded. **Results:** Demographic data were comparable. The mean time of Duration of Sensory Blockade in group M was 130.78±5.95 and in group C 165.02±12.72 (p value <0.001), mean time of 2 segment regression in group M was 103.44±8.01 and in group C 122.49±9.76 (p value <0.001), mean time of duration of motor blockade in group M is 144±6.78, in group C 208.27±21.39 (P value <0.001). Mean time onset of sensory block in group M was 9.44±0.69, in group C 5.85±0.32 (p value <0.001) were statistically significant. Hemodynamic parameters were comparable between the groups except at few intervals. Group C showed significant sensory and motor blockade and delayed requirement of rescue analgesia compared to group M. **Conclusion:** Intrathecal clonidine as adjuvant is better than intrathecal magnesium sulphate as it prolongs sensory and motor block with no significant haemodynamic variations and side affect.

Key Words: Spinal anaesthesia, Intrathecal adjuvants, Clonidine, Magnesium sulphate.

Introduction

Lower abdominal and lower limb surgeries may be performed under local, regional or general anaesthesia. First spinal anaesthesia was performed by August Bier in 1898 by using 0.5% cocaine. Spinal block is still the first choice because of its rapid onset, superior blockade, lower risk of infection, less failure rates and cost effectiveness but has drawbacks of shorter duration of block and less post operative analgesia. A wide variety of local anaesthetic drugs are available for spinal anaesthesia namely Lidocaine, Bupivacaine[1]. Lignocaine was the local anaesthetic of choice for decades due to its rapid onset of action and good motor block. But its use was limited by its short duration of action and its implication in causation of transient neurological symptoms and cauda equina syndrome following intrathecal injection[2].

*Correspondence
Dr. Vishwanath V.M
Senior Resident, Department of Anaesthesia, Shimoga Institute of Medical Sciences, Shimoga, Karnataka, India.
E-mail: Vm.vishwanath123@gmail.com

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[3].

Many adjuvants to local anaesthetic have been used intraoperative as well as post operative analgesia. Opioids are commonly used as intrathecal adjuvants to improve the quality of intraoperative analgesia and prolong it in post operative period without significant motor or autonomic blockade[4]. However pruritus, nausea, vomiting, respiratory depression and urinary retention are other common side effects for which search for ideal nonopioid adjuvants goes on[5].

In our study magnesium and clonidine is used as adjuvants for spinal anaesthesia. Magnesium prevents the development of central sensitization of pain by antagonistic action on N-methyl-D-aspartate receptors in the spinal cord. The calcium channel blocking property of magnesium also contributes to its antinociceptive effect[6].

Clonidine is a selective partial alfa2 adrenergic agonist. The activation of alfa2 adrenoreceptors by clonidine inhibits the central transmission of nociceptive impulses. The analgesic effect of clonidine is believed to result from inhibition of release of substance P.

Based on these evidences, study was conducted to evaluate and

compare the characteristics of spinal block and its side effects in adult patients undergoing infraumbilical surgeries who received a subarachnoid block with bupivacaine with either magnesium sulphate or clonidine.

Aims and objectives

To study the quality of subarachanoid block using intrathecal adjuvants magnesium sulphate and clonidine with hyperbaric bupivacaine in elective infraumbilical surgeries in terms of

- Time of onset of sensory and motor blockade.
- Total duration of sensory and motor blockade.
- Haemodynamic parameters.
- Side effects, if any.

Materials and methods

Source of data

The study was conducted on inpatients of Vanivilas hospital, Victoria hospital and Bowring hospitals attached to Bangalore Medical College and Research Institute, Bangalore.

Method of collection of data

Study design

A Prospective randomized double blind study.

Study period

The study was conducted over a period of two years from November 2017 to May 2019.

Sample size

Sample size was chosen based on outcome of previous study Mamtha khandelwal et al study considering duration of sensory block, keeping alpha error of 0.05, beta error at 0.2 and 80% power and expected minimum difference of 12mins the sample size is 45 in each group.

Inclusion criteria

a) Patient who gave written informed consent
b) Patients aged 18 - 60 yrs of either sex.
c) Patients with ASA grade1&2.
d) Patients posted for elective infraumbilical surgeries.

Exclusion criteria

a) Patient refusing to participate in the study.
b) ASA grade 3 and above.
c) Age < 18 and > 60 years.
d) Patients who were morbidly obese and under nourished..
e) Respiratory insufficiency.
f) Allergy to local anesthetics, magnesium sulphate and clonidine.
g) Uncontrolled diabetes mellitus, hypertension, recent myocardial infarction.
h) Contraindications/relative contraindications to spinal anaesthesia.
i) Hypovolaemic shock, Bleeding diathesis and coagulopathy.
j) Psychiatric disorder.

Anaesthetic procedure

After obtaining clearence and approval from Institutional Ethical Commitee, patients fulfilling inclusión criteria who gave informed consent (ANNEXURE 1) were included in the study and were randomised using numbers generated from www.random.org website and divided into two groups,

1. Group M (n=45) : Bupivacaine (0.5% H) 2.5 ml + Magnesium Sulphate 30mg.
2. Group C (n=45) : Bupivacaine (0.5% H) 2.5 ml + Clonidine 30mcg.

Both group volume made equal to 3ml by adding normal saline

A routine pre-anaesthetic examination was conducted on the evening before the scheduled day of surgery, assessing:

- History and general condition of the patient
- Airway assessment by Mallampatti grading
- Nutritional status, height and weight of the patient
- A detailed examination of the systems like cardiovascular system, Respiratory system and Central nervous system.
- Examination of the Spine.

The following investigations were done in all patients

- Complete blood count
- Random blood sugar
- Serum electrolytes, Renal Function Tests
- Urine Routine Examination
- Standard 12-lead Electrocardiogram
- Chest X ray

All patients were kept fasting for 8 hours on the previous day of surgery. Patients were pre medicated with tab Alprazolam 0.25mg and tab Ranitidine150 mg on the night before the day of surgery. On the day of surgery, in preoperative room, intravenous line was secured with 18G I.V. cannula and were preloaded with 10 ml/kg of Ringer Lactate. Injection Ranitidine 50mg was given intravenously half an hour preoperatively.

On the arrival to the operating room, Non invasive blood pressure, pulse oximeter and three lead Electrocardiogram were connected. The baseline systolic, diastolic blood pressure (SBP, DBP), heart rate (HR) and oxygen saturation (SpO2) were recorded.

Under strict aseptic precautions subarachnoid block was performed by using 25 G Quincke Babcock spinal needle in the L2- L3 interspace with patient in left lateral position. The study drug was loaded in a 5ml syringe by a senior anaesthesiologist who was not involved in the study. Just before spinal anaesthesia, syringe was handed over to the anaesthesiologist performing the subarachnoid block, who was also the observer of the study. The patients were not aware of the drug being administered to them. Thus both the observer and the patient were blinded. The study drug was injected over 10-15 seconds. The time at which injection was completed was considered as zero time of the study and all measurements were recorded from this point. Patients were made to lie down in the supine posture immediately after the subarachnoid injection of the study drug, keeping the table flat. All patients were given supplementary oxygen through a venturi mask at 5L/min.

Sensory testing was assessed by loss of pinprick sensation to 23 G sterile hypodermic needle for the onset and dermatomal levels were tested every 2 minutes until the highest level had been achieved and stabilized for four consecutive tests. Time of onset of motor block was assessed by using Modified Bromage Scale (ANNEXURE 3). Intraoperatively, vital parameters like heart rate, non-invasive blood pressure and percentage of oxygen saturation and will be recorded every 2 minute for the first 10 minutes, then every 5 minutes till 1 hour of surgery and then every 10 minutes till the end of surgery. Postoperatively, every 1 hour for 24hrs.

Hypotension was defined as 20% fall in systolic blood pressure from baseline and was treated with intravenous fluids and intravenous injection Mephenteramine 6mg. Bradycardia was defined as 20% fall in heart rate from baseline and was treated with intravenous injection Atropine 0.6 mg.

Data regarding the time to reach highest dermatomal level of sensory blockade from the time of injection, time for sensory regression at L1 were recorded. In case of failure of subarachnoid block and conversion to general anaesthesia, were excluded from the study.

After the surgery, patients were shifted to the post anaesthesia care and recovery unit where they remained until complete recovery of sensory and motor blockade was achieved. Post operatively, the hemodynamic variables and oxygen saturation were recorded upto 24 hours postoperatively. The incidence of any adverse effects such as hypotension, bradycardia, shivering, nausea, vomiting, pruritis, respiratory depression and ECG changes were noted and treated.

Definitions of various parameters studied

Onset of sensory blockade: was defined as time taken from the completion of the injection of the study drug till the patient did not feel pin prick sensation at L1 dermatome.

Maximum height of sensory blockade achieved: was defined as the maximum sensory blockade attained from the time of completion of injection of study drug.

Duration of sensory block: was defined as the time taken from the onset of sensory blockade at L1 level till the sensory level receded to below L1 dermatome level.

Onset of motor blockade: was defined as the time taken from the completion of the injection of study drug till the patient achieved motor blockade of Bromage score 3.

Duration of motor blockade: was defined as the time taken from the onset of motor blockade of Bromage score 3 till the complete recovery of motor blockade to Bromage score 0.

Time for two segment regression from highest sensory level: is the time in minutes taken to regress the level of loss of pin prick sensation achieved to two lower sensory dermatomal levels. This will be taken as total duration of analgesia

Time for Rescue analgesia time: is the time taken in minutes from the time of injection to the time when the patient complains of pain at surgical site, VAS>4(Annexure 4). This defines the total duration of sensory blockade.

Efficacy parameters are assed as follow:**Duration of motor blockade** assessed by Modified Bromage Scale (ANNEXURE 3).

Pain intensity measured using visual analog scale(VAS) (ANNEXURE 4).

Sedation assessed with Ramsay Sedation Scale (ANNEXURE 5) and recorded. Score of 4 and above is considered as sedated.

Duration of complete analgesia assessed from the time of onset of analgesia till the appearance of pain for first time (first rescue analgesic). Rescue analgesia provided with interventional analgesics.

Any complications occurred in the first post-operative week that is communicated to us was documented.

Sample size estimation

Sample size

Sample size was chosen based on outcome of previous study Mamtha khandelwal et al study considering duration of sensory block, keeping alpha error of 0.05, beta error at 0.2 and 80% power and expected minimum difference of 12mins the sample size is 45 in each group.

The sample size calculation

$n= 2(Z\alpha+ Z_{1-\beta})^2 \sigma^2 / d^2$

Demography

Where Zα= standard table value for 95% CI =1.96

$Z_{1-\beta}$ = Standard table value for 80% Power = 0.84

σ = Standard Deviation = 19

d=Effect Size= 12

$n= 2(1.96+ 0.84)^2 (19)^2 / (12)^2$

n=43

n = 45

We are taking sample size 45 in each group.

Statistical analysis

Data was entered into Microsoft excel data sheet and was analyzed using SPSS 22 version 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.

Graphical representation of data

MS Excel and MS word was used to obtain various types of graphs such as bar diagram, line diagram.

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.

Results

It is a prospective randomized controlled study with 90 patients randomly divided into two groups of 40 patients each, using www.random.org.

1. Group M (n=45) : Bupivacaine (0.5% H) 2.5 ml + Magnesium Sulphate 30mg.
2. Group C (n=45) : Bupivacaine (0.5% H) 2.5 ml + Clonidine 30mcg.

Both group volume made equal to 3ml by adding normal saline

Patients were evaluated for onset and duration of sensory and motor blockade, dermatomal level achieved, hemodynamic variations and side effects of the drug if any.

Table 1: Gender distribution comparison between two groups

		Group					
		Group C		Group M		Total	
		Count	%	Count	%	Count	%
Sex	Female	22	48.89%	20	44.44%	42	46.67%
	Male	23	51.11%	25	55.56%	48	53.33%
	Total	45	100.00%	45	100.00%	90	100.00%

χ 2 = 0.179 , df = 1, p = 0.673

In Group C, 51.11% were males and 48.89% were females and in Group M, 55.56% were males and 44.44% were females. There was no significant difference in sex distribution between two groups.

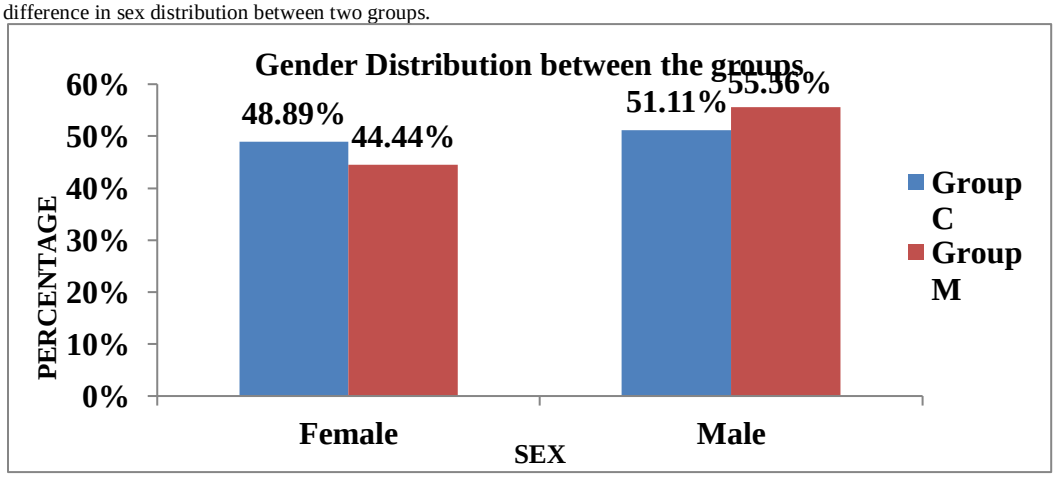

Fig 1: Bar diagram showing gender distribution between the groups in study subjects

Table 2: Age (in years) distribution comparison between two groups

		Group					
		Group C		Group M		Total	
		Count	%	Count	%	Count	%
Age	20 - 30 Years	2	4.44%	3	6.67%	5	5.56%
	31 - 40 Years	18	40.00%	19	42.22%	37	41.11%
	41 - 50 Years	21	46.67%	20	44.44%	41	45.56%
	> 50 Years	4	8.89%	3	6.67%	7	7.78%
	Total	45	100.00%	45	100.00%	90	100.00%

χ 2 = 0.394 , df = 3, p = 0.941

In Group C, majority of subjects were in the age group 41 to 50 years (46.67%), in Group M, majority of subjects were in the age group 41 to 50 years (44.4%). There was no significant difference in age distribution between two groups.

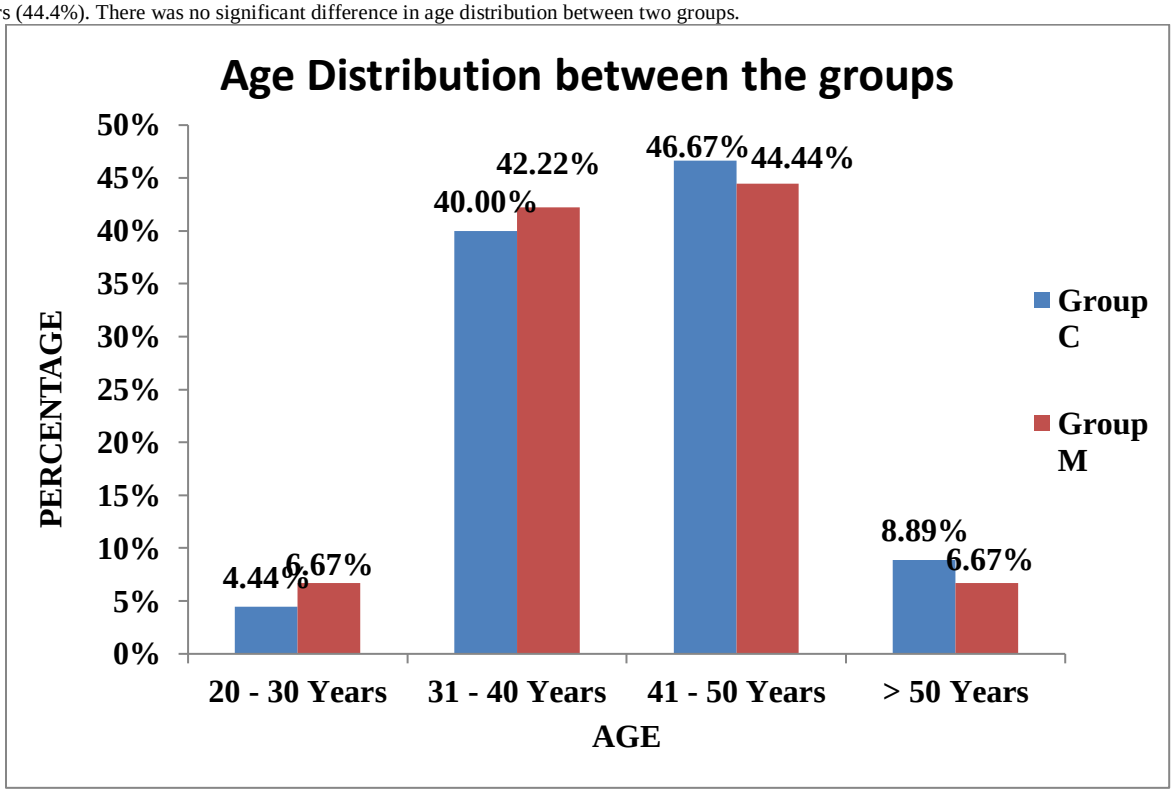

Fig 2: Bar diagram showing age distribution between the groups in study subjects

Table 3: Mean Age, Weight and Height and BMI comparison between two groups

	Group						P value
	Group C		Group M		Total		
	Mean	SD	Mean	SD	Mean	SD	
Age	41.11	7.12	41.07	6.72	41.09	6.88	0.976
Weight (Kg)	62.71	8.18	61.67	6.73	62.19	7.47	0.510
Height (M)	1.60	.05	1.61	.05	1.60	.05	0.324
BMI	24.54	2.59	23.83	2.10	24.18	2.37	0.159

In the study there was no significant difference in mean age, weight, Height and BMI between two groups.

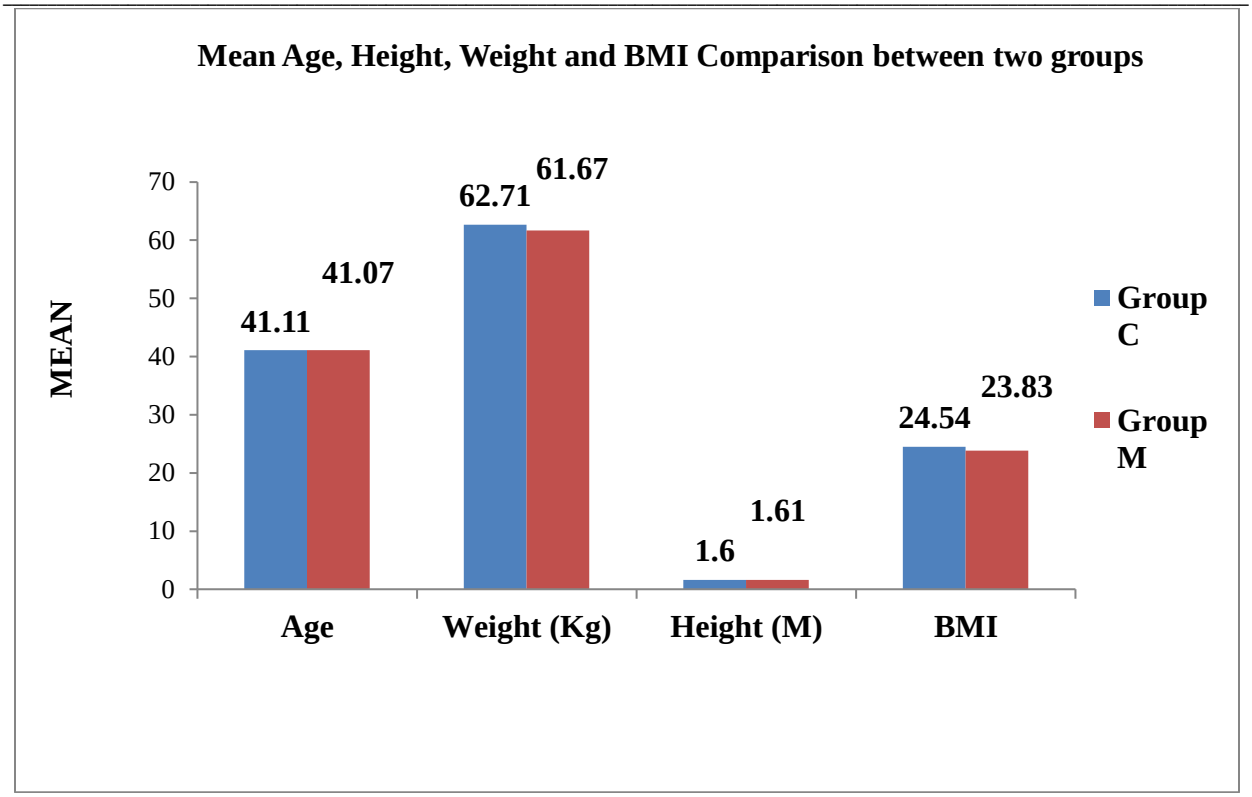

Fig 3: Bar diagram showing mean age, height, weight and BMI Comparison between two groups

Table 4: ASA grade comparison between two groups

		Group					
		Group C		Group M		Total	
		Count	%	Count	%	Count	%
ASA	1	30	66.67%	30	66.67%	60	66.67%
	2	15	33.33%	15	33.33%	30	33.33%

χ 2 = 0.000 , df = 1, p = 1.000

In both the groups, 66.67% had ASA grade 1 and 33.3% had ASA grade 2. There was no significant difference in ASA grade between two groups.

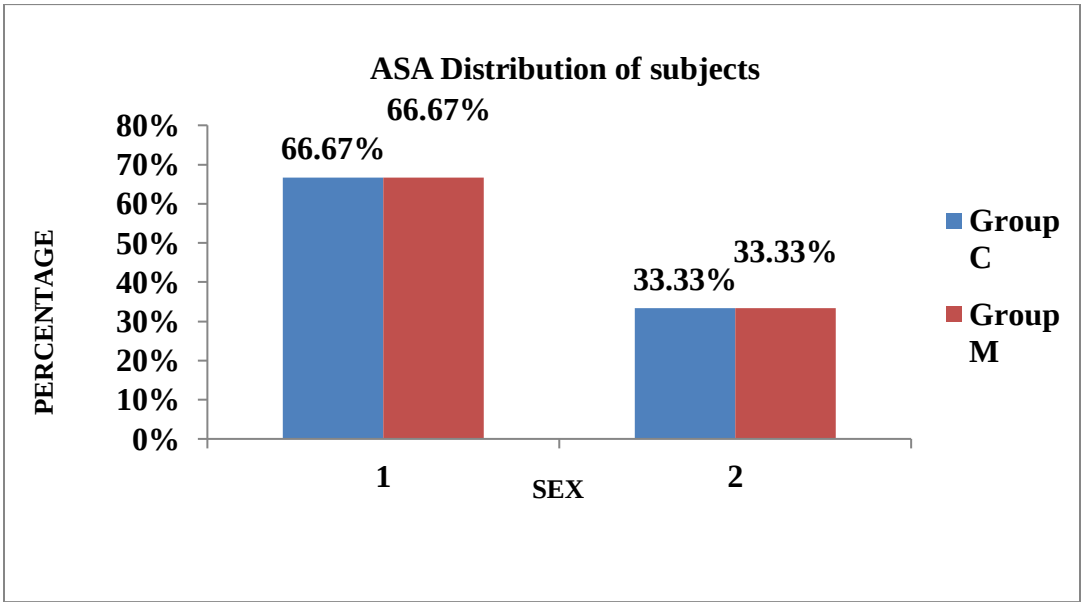

Fig 4: Bar diagram showing ASA distribution between 2 groups.

Table 5: Mean onset of sensory block duration comparison between two groups

	Group						P Value
	Group C		Group M		Total		
	Mean	SD	Mean	SD	Mean	SD	
At L1 (Minutes)	3.84	.45	6.66	.42	5.25	1.48	< 0.001*
At Highest Sensory LEVEL(Minutes)	5.85	.32	9.44	.67	7.64	1.88	< 0.001*

In Group C, mean onset of sensory block at L1 was 3.84 ± 0.45 min and in Group M was 6.66 ± 0.42. There was significant difference in Mean onset of sensory block between two groups.
In Group C, mean onset of sensory block at highest sensory level was 5.85 ± 0.32 min and in Group M was 9.44 ± 0.67. There was significant difference in Mean onset of sensory block at highest sensory level between two groups.

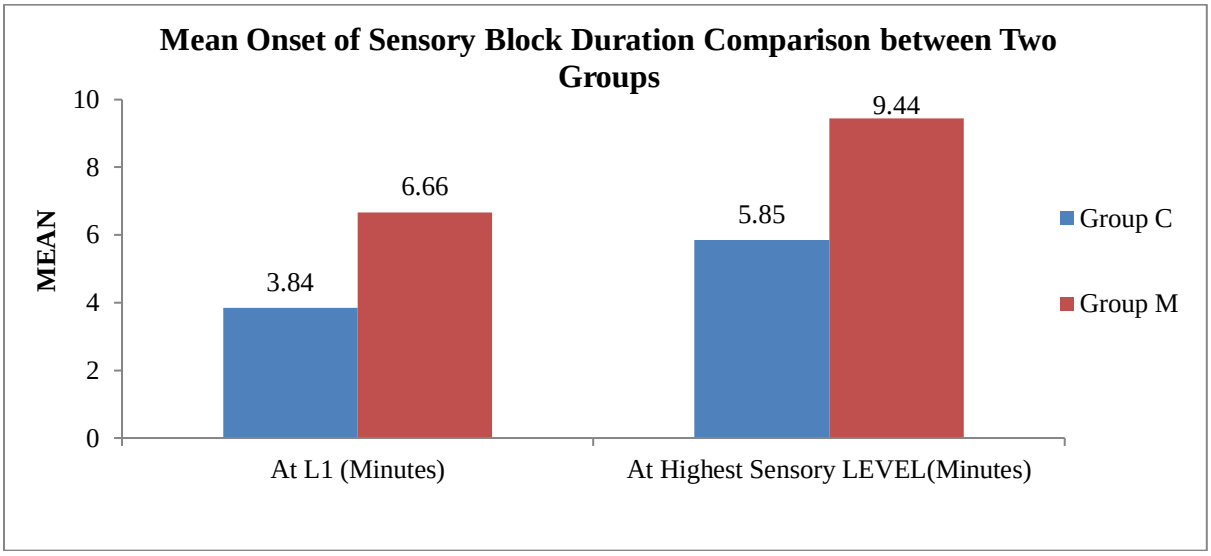

Fig 5: Bar diagram showing mean onset of sensory block duration comparison between two groups in study subjects

Table 6: Max Ht of Sensory Block Distribution between two groups

		Group					
		Group C		Group M		Total	
		Count	%	Count	%	Count	%
Max Ht Of Sensory Block	T4	1	2.22%	1	2.22%	2	2.22%
	T6	19	42.22%	19	42.22%	38	42.22%
	T7	9	20.00%	8	17.78%	17	18.89%
	T8	16	35.56%	17	37.78%	33	36.67%

χ 2 = 0.089 , df = 3, p = 0.993
In Group C, majority of subjects had maximum height of sensory block at T6 (42.22%) and in Group M, majority of subjects had maximum height of sensory block at T6 (42.22%).There was no significant difference in Max Ht Of Sensory Block between two groups.

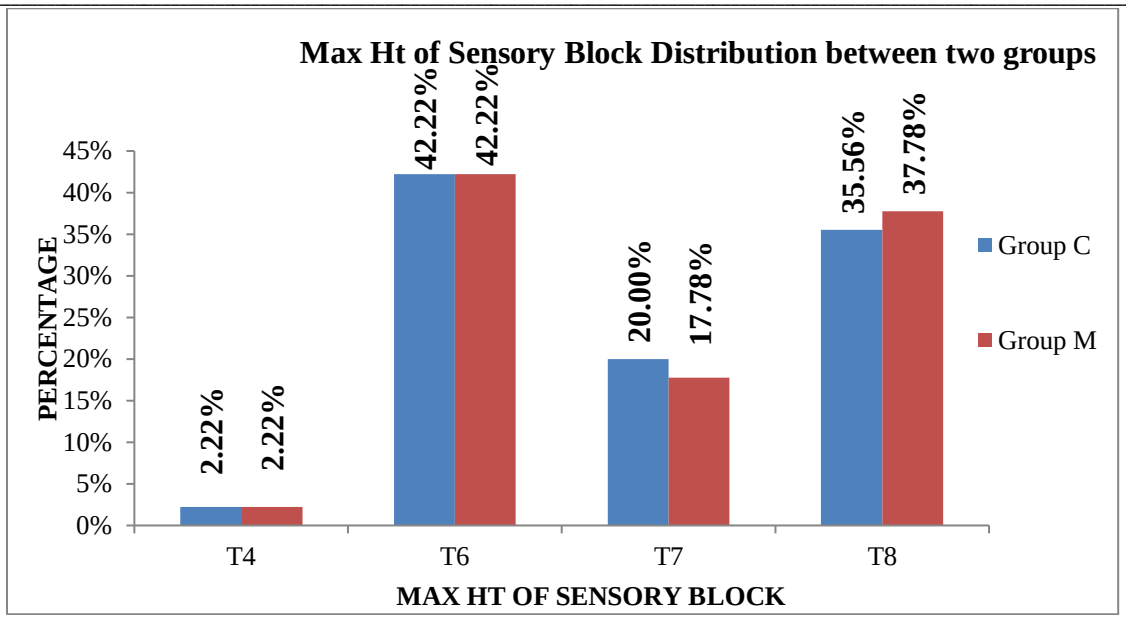

Fig 6: Bar diagram showing max Ht Of sensory block distribution between two groups.

Table 7: Mean of Dermatome Sensory Block Regression Time, Total Duration Of Sensory Block, Onset Of Motor Block, Duration Of Motor Block, Time For First Analgesic Dose Comparison between two groups

	Group						P Value
	Group C		Group M		Total		
	Mean	SD	Mean	SD	Mean	SD	
2 Dermatome Sensory Block Regression Time (Minute)	122.49	9.76	103.44	8.01	112.97	13.06	< 0.001*
Total Duration Of Sensory Block (Minute)	165.02	12.72	130.78	5.95	147.90	19.85	< 0.001*
Onset Of Motor Block (Minutes)	4.67	0.86	8.72	1.69	6.70	2.43	< 0.001*
Duration Of Motor Block (Minutes)	208.27	21.39	144.00	6.78	176.13	35.96	< 0.001*
Time For First Analgesic Dose (Minutes)	176.29	14.45	140.76	16.17	158.52	23.49	< 0.001*

In the study there was significant difference in mean 2 Dermatome Sensory Block Regression Time, Total Duration Of Sensory Block, Duration Of Motor Block and Time For First Analgesic Dose between two groups. All the above parameters were significantly higher in Group C compared to Group M. Mean Onset of Motor Block was significant faster in Group C compared to Group M. There was significant difference in mean Onset of Motor Block between two groups.

Table 8: Mean Pulse Comparison between two groups at different time interval

Pulse	Group				P Value
	Group C		Group M		
	Mean	SD	Mean	SD	
Baseline	83.18	8.28	83.58	9.02	0.827
2min	83.13	7.23	82.51	8.67	0.712
4min	79.69	7.08	80.56	7.87	0.584
6min	77.22	7.41	79.31	7.98	0.202
8min	75.04	7.25	78.82	8.69	0.028*
10min	72.24	7.20	77.38	8.20	0.002*
15min	70.04	7.47	76.27	8.80	0.001*
20min	68.04	8.05	75.87	9.58	< 0.001*
25min	65.89	8.41	75.98	9.27	< 0.001*
30min	64.51	8.12	76.78	9.16	< 0.001*
35min	63.68	8.47	76.14	9.40	< 0.001*
40min	62.53	8.68	75.02	7.51	< 0.001*
45min	62.26	8.44	75.42	7.46	< 0.001*
50min	62.45	9.20	73.76	8.38	< 0.001*
55min	61.70	7.46	76.10	9.18	< 0.001*
60min	61.31	6.28	76.18	8.18	< 0.001*
75min	61.55	6.12	74.50	8.02	< 0.001*
90min	61.47	6.38	75.92	4.80	< 0.001*
105min	64.50	8.47	76.57	3.64	0.004*
120min	62.40	7.70	63.00	1.41	0.921
Immediate Post Op	71.29	8.98	70.98	7.26	0.857
1hr	71.64	9.43	71.51	5.91	0.936

2hr	74.44	6.49	73.56	6.28	0.511
3hr	73.82	6.41	75.18	6.18	0.310
4hr	76.16	4.72	77.64	6.45	0.215
8hr	78.98	5.73	79.27	6.91	0.830
12hr	77.49	6.10	80.18	6.95	0.054
16hr	80.71	6.59	81.22	8.69	0.754
20hr	82.33	6.39	82.47	9.23	0.937
24hr	82.56	6.97	83.71	9.19	0.503

In the study there was significant difference in mean PR between two groups from 8 min to 105 min. At these intervals mean HR was significantly higher in Group M compared to Group C. At other intervals there was no significant difference in mean PR between two groups

Table 9: Mean SBP comparison between two groups at different time intervals

SBP	Group				P Value
	Group C		Group M		
	Mean	SD	Mean	SD	
SBP Baseline	131.98	10.62	133.13	10.53	0.606
2min	117.20	11.06	116.69	13.63	0.846
4min	105.27	8.96	109.84	12.57	0.050
6min	101.07	8.66	106.22	12.41	0.025*
8min	97.13	8.49	104.33	11.42	0.001*
10min	96.69	8.09	102.02	11.47	0.013*
15min	95.76	9.96	99.96	11.57	0.068
20min	96.24	10.73	102.31	11.90	0.013*
25min	99.60	9.26	103.04	11.64	0.124
30min	101.80	9.59	102.64	11.04	0.699
35min	103.56	9.90	102.82	10.62	0.738
40min	104.73	11.36	104.60	12.08	0.961
45min	105.26	10.22	106.29	11.72	0.692
50min	106.56	13.13	108.29	12.03	0.582
55min	106.77	11.86	108.31	11.53	0.614
60min	107.32	9.60	109.62	11.42	0.427
75min	107.33	9.28	108.36	9.74	0.715
90min	106.83	8.96	107.39	7.87	0.859
105min	111.43	13.09	111.88	10.60	0.943
120min	108.00	4.24	110.80	12.64	0.782
Immediate Post OP	113.69	13.76	119.69	11.77	0.029*
1hr	118.33	9.32	122.58	9.73	0.037*
2hr	121.13	8.38	124.84	9.16	0.048*
3hr	122.62	8.36	125.11	11.42	0.241
4hr	123.91	10.49	125.91	11.18	0.384
8hr	124.00	9.89	126.24	11.51	0.324
12hr	119.36	17.71	125.11	12.62	0.079
16hr	122.93	10.38	123.44	13.07	0.838
20hr	124.80	8.96	125.36	11.62	0.800
24hr	128.49	9.20	127.98	10.62	0.808

In the study there was significant difference in mean SBP between two groups from 6 min to 10 min, at 20 min, from immediate post op to 2 hr post op. At these intervals SBP was lower in Group C compared to Group M. At other intervals there was no significant difference in mean SBP between two groups.

Table 10: Mean DBP Comparison between two groups at different time interval

DBP	Group				P Value
	Group C		Group M		
	Mean	SD	Mean	SD	
DBP Baseline	75.51	10.15	76.71	8.44	0.544
2min	63.33	9.89	65.00	6.49	0.347
4min	60.31	9.06	60.47	5.95	0.924
6min	57.00	8.93	58.13	6.18	0.486
8min	55.69	8.76	55.84	5.90	0.922
10min	53.98	8.57	55.98	8.09	0.258
15min	53.44	9.68	54.69	8.18	0.512
20min	54.29	8.96	53.64	9.48	0.741
25min	53.40	7.48	52.36	9.12	0.554
30min	53.49	7.17	53.38	9.26	0.949
35min	53.98	6.84	54.21	8.64	0.890
40min	53.37	6.34	54.41	9.45	0.553

45min	54.66	6.83	54.68	7.77	0.987
50min	55.61	6.47	55.68	9.23	0.975
55min	55.59	7.32	57.47	10.51	0.430
60min	55.65	7.31	56.50	9.48	0.716
75min	56.14	6.70	55.71	6.80	0.831
90min	56.83	5.29	54.83	8.02	0.416
105min	58.50	4.00	56.71	4.61	0.436
120min	61.60	4.93	57.50	10.61	0.483
Immediate Post OP	65.58	8.56	62.20	6.70	0.040*
1hr	68.16	6.18	65.93	5.33	0.071
2hr	69.29	6.06	67.51	5.87	0.161
3hr	69.04	8.51	67.42	6.22	0.305
4hr	67.78	8.12	67.13	6.20	0.673
8hr	67.49	8.85	69.71	6.38	0.175
12hr	68.93	8.13	69.69	5.27	0.602
16hr	69.18	7.40	72.07	7.08	0.062
20hr	69.71	7.62	74.51	8.63	0.006*
24hr	69.93	7.35	79.91	10.19	< 0.001*

In the study there was significant difference in mean DBP between two groups at Immediate Post OP, 20 hr and 24 hrs. Mean DBP at these intervals was significantly lower in Group C compared to Group M. At other intervals there was no significant difference in mean DBP between two groups.

Table 11: Mean MAP Comparison between two groups at different time interval

MAP	Group				P Value
	Group C		Group M		
	Mean	SD	Mean	SD	
MAP Baseline	94.33	8.92	95.52	7.84	0.505
2min	81.29	8.78	82.23	6.89	0.573
4min	75.30	7.03	76.93	6.02	0.240
6min	71.69	7.61	74.16	6.16	0.093
8min	69.50	7.52	72.01	5.83	0.081
10min	68.21	7.22	71.33	7.49	0.048*
15min	67.55	8.73	69.78	7.53	0.198
20min	68.27	8.57	69.87	9.09	0.395
25min	68.80	7.04	69.25	8.16	0.779
30min	69.59	6.38	69.80	8.70	0.898
35min	68.90	9.52	69.59	9.65	0.737
40min	67.30	11.09	67.88	13.39	0.827
45min	63.63	15.43	64.03	16.13	0.907
50min	62.03	17.31	62.66	18.23	0.877
55min	61.21	17.48	62.75	17.37	0.712
60min	60.32	19.52	62.65	16.76	0.611
75min	60.07	17.20	60.21	16.82	0.975
90min	55.47	18.68	54.15	19.57	0.829
105min	63.56	16.16	62.56	17.82	0.902
120min	55.47	19.43	52.27	23.05	0.818
Imm. Postop	81.61	6.35	81.36	5.21	0.837
1hr	84.88	5.16	84.81	4.66	0.949
2hr	86.57	5.04	86.62	5.09	0.961
3hr	86.90	6.80	86.65	6.94	0.862
4hr	94.66	56.40	86.73	6.89	0.352
8hr	86.33	7.55	88.56	6.59	0.139
12hr	85.74	8.71	88.16	5.91	0.126
16hr	95.62	58.03	89.19	7.00	0.463
20hr	88.07	6.12	101.67	69.67	0.196
24hr	89.45	5.30	95.93	7.01	< 0.001*

In the study there was significant difference in mean MAP between two groups at 10min and 24hr post op. At these intervals mean MAP was significantly lower in Group C compared to Group M. At other intervals there was no significant difference in mean MAP between two groups.

Table 12: Mean RR Comparison between two groups at different time interval

	Group				P Value
	Group C		Group M		
	Mean	SD	Mean	SD	
RR Baseline	14.89	1.210	14.51	1.604	0.211
RR at Immediate Post op	14.82	1.193	14.44	1.374	0.167
RR Post Op	13.80	1.27	13.36	1.17	0.088

In the study there was no significant difference in mean RR at baseline, at Immediate Post op period between two groups.

Table 13: Mean Ramsey Sedation Score Comparison between two groups at different time interval

Ramsey Sedation Score	Group				P Value
	Group C		Group M		
	Mean	SD	Mean	SD	
Baseline	1.91	.47	1.62	.49	0.005*
5min	2.49	.51	1.82	.39	< 0.001*
10min	2.82	.39	2.09	.42	< 0.001*
20min	2.78	.42	2.16	.37	< 0.001*
40min	2.53	.50	2.02	.15	< 0.001*
60min	2.23	.43	2.08	.27	0.076
80min	2.04	.20	2.00	.00	0.323
100min	2.00	.00	2.00	.00	-
120min	2.00	.00	1.67	.58	0.170
Immediate Post Operative	2.00	.00	1.91	.29	0.041*
1hr	2.00	.00	1.91	.29	0.041*
2hr	2.00	.00	1.98	.15	0.320
6hr	2.00	.00	1.91	.29	0.041*
12hr	1.87	.34	1.89	.32	0.751
24hr	1.82	.39	1.96	.21	0.045*

In the study there was significant difference in mean Ramsay sedation score between two groups from baseline to 24 hr post op. Mean RSS was higher in Group C than in Group M.

Table 14: Mean VAS Score Comparison between two groups

VAS Score	Group				P Value
	Group C		Group M		
	Mean	SD	Mean	SD	
Immediate Post Operative	.22	.42	.62	.75	0.002*
1hr	1.93	.65	2.71	.97	< 0.001*
2hr	3.02	.92	4.78	1.02	< 0.001*
6hr	6.20	.73	6.49	.51	0.031*
12hr	5.73	.84	5.40	.58	0.031*
24hr	5.64	.91	5.24	.53	0.012*

In the study there was significant difference in mean VAS score between two groups from immediate post op to 24 hr post op period. Mean VAS score was higher in Group M from Immediate post op to 6 hr from 12 hr to 24 hr Mean compared to group C.

Table 15: Bradycardia Distribution (Considered heart rate less than 50) between two groups

In the study there was no significant difference in Bradycardia between two groups at all the intervals.

Bradycardia	Group				P Value
	Group C		Group M		
	Count	%	Count	%	
30min	1	2.22%	0	0.00%	0.320
35min	1	2.27%	0	0.00%	0.326
40min	2	4.65%	0	0.00%	0.166
55min	2	6.67%	0	0.00%	0.155

Table 16: Hypotension Distribution (Considered systole less than 80) between two groups

In the study there was no significant difference in incidence of Hypotension between two groups at all the intervals of follow-up.

Hypotension	Group				P Value
	Group C		Group M		
	Count	%	Count	%	
10min	1	2.22%	0	0.00%	0.320
15min	2	4.44%	3	6.67%	0.650
20min	0	0.00%	1	2.22%	0.320
25min	1	2.22%	0	0.00%	0.320
35min	0	0.00%	1	2.33%	0.315
12hr	0	0.00%	1	2.22%	0.320

Discussion

Sample size was chosen based on outcome of previous study considering duration of sensory block, keeping alpha error of 0.05, beta error at 0.2 and 80% power and expected minimum difference of 12mins the sample size was 43, for better outcome sample size taken as 45 in each group.

Hypothesis made before starting the study

We hypothesized that clonidine administered along with hyperbaric bupivacaine in subarachnoid blockade for infraumbilical surgeries would have longer duration of analgesia compared to magnesium sulphate with hyperbaric bupivacaine.

In this clinical study of patients posted for various infraumbilical surgeries belonging to ASA 1 and 2 selected.

1.Group M (n=45) - Bupivacaine (0.5% H) 2.5ml with magnesium sulphate 30mg
2.Group C (n=45) - Bupivacaine (0.5% H) 2.5ml with clonidine 30 µg.
Volum made equal to 3ml by adding normal saline in each group.
Demographic data comparing age, gender, weight, height, ASA grade shows no statistically significant difference among both the groups.

Onset of sensory and motor blocked

Onset of sensory block

In our study Group C, mean onset of sensory block at L10 was 3.84 ± 0.45 min and in Group M was 6.66 ± .42min. There was significant (p<0.001) difference in Mean onset of sensory block between two groups. Mean onset of sensory block at highest sensory level in group C was 5.85 ± 0.32 min and in Group M was 9.44 ± 0.67. There was significant (p<0.001) difference in Mean onset of sensory block at highest sensory level between two groups.

Onset of motor block

In group C onset of sensory blocked was 4.67 ± 0.86 min which was significantly (p<0.001) faster than group M 8.72 ± 1.69 min.
There was significant delay in onset of both sensory and motor onset in group M compared to group C.
In Mamta khandelwal at al[6]. study they have measured highest level of sensory blocked. Onset of both sensory and motor block (4 ± 0.8 min and4 ± 0.7 min) was significantly (p<0.001) faster in group C (clonidine 30mcg) compared to gropup M (7.1± 2.5min and 8.5 ± 3.6 min) which has magnesium sulphate 50 mg as adjuvant and group B (6 ± 1.2 min and 6.7 ± 1.4 min) which has normal saline as adjuvant, whereas Group M showed the significantly delayed onset of both sensory (P = 0.033) and motor (P = 0.007) blockade compared to Group B.

2 dermatome sensory block regression time and total duration of sensory block

Group C, mean of Two Dermatome sensory block regression time was 122.49 ± 9.76 min, mean Total Duration of Sensory Blockade was 165.02 ± 12.72 min. In Group M, mean of Two Dermatome sensory block Regression time was 103 ± 8.01 min, mean Total Duration of Sensory Blockade was 130.78 ± 5.95 min. There was significant (p<0.001) difference in mean of Two Dermatome sensory block Regression and mean of taotal Duration of Sensory Blockade. Group C has prolonged total duration of sensory blockade and 2 dermatome sensory regression was also delayed compared to group M.
In study conducted by M Khandelwal at al[6]. Concluded that total duration of sensory block in group B (normal saline) was 94 ± 24.4min, in group C (clonidine) 166.5 ± 23.3 min and in group M (magnesium) 123 ± 16.6mins. group C has significant (<0.01) longer duration of total sensory block comapred to group M, and both group C and M has significant longer duartion of sensory blockade compared with group B. which supports our study.
In study conducted by Binesh Kathuria et al. the duration of sensory block was defined as time of regression of twosegment in the maximum sensory block height, evaluated by pin prick. Group II III receiving magnesium sulphate showed prolonged sensory blockade compared to group I received normal saline as adjuvant. Hence the study proved that magnesium sulphate as adjuvant prolongs the total duration of sensory blockade compared to the group with normal saline as adjuvant.
Tilkar Y etal using 50µg of fentanyl and 150µg of clonidine with 15mg of hyperbaric bupivacaine for orthopaedic procedures which are higher dosages than our study dosage of adjuvants showed time taken for regression of sensory block to below T10 was significantly more in clonidine group (362.9+/-13min) than fentanyl group (272.9+/-15.6 min) which is consistent our study results where we have taken two segment regression instead of level below T10 and also duration of analgesia (from subarachnoid injection to first report of pain in min) is more in group C (387.8+/-14 min) compared to group F (177+/-23.6 min).

Total duration of motor blockade

In this study duration of Motor Blockade in group C was 208.27 ± 21.39 min and mean Duration of Motor Blockade in group M was 144 ± 6.78 min. group C showed significant (p<0.001) longer duration of motor block compared to group M.
In M Khandelwal et al. study total duration of motor block in group B was 116.3 ± 16.4 min and in group C 218.5 ±52.7min and in group M 138.3 ±25.7min. group C showed significant longer motor blocked compared to both group M and B.

Time of request for first analegesic dose

In Group C, mean time taken for First Analgesic was 176.29 ± 14.45 min and in Group M 140.76 ± 16.17 min. There was significant difference in mean Time for First Analgesic between two groups.
In M Khandelwal et al[6].study The duration of analgesia (time to first rescue analgesia) was significantly (P < 0.01) prolonged in Group C (330.7 ± 47.7 min) compared to both Group M (246.2 ± 55.9 min) and Group B (134.4 ± 17.9 min), and Group M showed a significantly (P < 0.01) longer duration of analgesia compared to Group B. which isn support to our study.

Hemodynamic variations

In the study, there was significant difference in mean PR between two groups from 8 min to 105 min. At these intervals mean HR was significantly lower in Group C compared to Group M. At other intervals there was no significant difference in mean PR between two groups. But it dint require any intervention and treatment.
In Tilkar Y etal study used 50µg of fentanyl and 150µg of clonidine with 15mg of hyperbaric bupivacaine for orthopaedic procedures incidence of hypotension and also bradycardia was found significant in group C (P < 0.05) compared to group F which concurs with our study with much lower dosage of adjuvants however most of the fall in blood pressure and fall in heart rate in clonidine group didn't require any treatrment. Therefore the risk of hypotension requiring treatment increased with increase in dosage.
Where as in study conducted by M Ozalevali at al. where they used magnesium 50mg as intrathecal adjuvant for bupivacain-fentanyl prepration found out no significant changes were seen in HR or MAP.

Other side effects

The sedative effect of clonidine is dose dependent. In our study group C shows significant sedation comopared to the group M mainly in intraoperative first 60mins.
In contrast study of M Khandelwal at al[6] used 30mcg of clonidine dint find any intraoperative or post operative significant sedation in clonidine group.
In Tilkar Y etal study showed incidence of hypotension and bradycardia requiring treatment and also sedation was significant in clonidine group compared fentanyl, where they have used higher doses of clonidine compared to our study dosage of adjuvants.
In M Khandelwal at al[6].study among three groups, VAS was significantly different (P < 0.001) from 30 min to 120 min whereas Group B showed significantly (P < 0.05) higher values of VAS compared to other two groups. The patients of Group M showed a significantly (P < 0.05) higher level of VAS compared to Group C at 60 min, 90 min and 120 min.

Limitations of the study

If taken equipotent dose of both clonidine and magnesium sulpate used, study would have been more accurate. We have not calculated total dose of rescue analgesia consumed post operatively in both the groups, which would have given accurate extra dose requirement of additional analgesia in group M.

Conclusion

To conclude, our study demonstrates that intrathecal clonidine as

adjuvant is better than magnesium sulphate with 0.5% bupivacaine as it provides better post operative analgesia and with minimal haemodynamical variatrion and no side effects.

References

1. Corby MP, Bach AB. Transient radicular irritation (TRI) after spinal anaesthesia in day - care surgery. Acta Anaesthes Scand 1998; 42: 425-9.
2. Henderson DJ, Faccenda KA, Morrison LM. Transient radicular irritation with intrathecal plain lignocaine. Acta Anaesthesiol Scand 1998; 42: 376-8.
3. Richard Brull, Alan J.R, MacFarlane Vincent W.S.Chan. Spinal, Epidural, and Caudal Anaesthesia. In: Ronald D. Miller editor. Miller's Anaesthesia 8th ed. Philadelphia Elsevier Saunders; 2015:1698-1699.
4. Tony L Yaksh, Mark S. Wallace. Opioids, Analgesia, and Pain Management. In: Laurence L. Brunton, editor. Goodman & Gilman's The Pharmacological Basis of Therapeutics. 12th ed. New York Mc Graw Hill;2011:510.
5. Routray SS, Raut K, Pradhan A, Dash A, Soren M. Comparison of intrathecal clonidine and fentanyl as adjuvants to hyperbaric bupivacaine in subarachnoid block for lower limb orthopedic surgery. Anesth Essays Res. 2017 J;11(3):589-93.
6. Khandelwal M, Dutta D, Bafna U, Chauhan S, Jetley P, Mitra S. Comparison of intrathecal clonidine and magnesium sulphate used as an adjuvant with hyperbaric bupivacaine in lower abdominal surgery. Indian J Anaesth.2017;61:667-72.
7. Eisenach JC, De Kock M, Klimscha W. Alpha (2) adrenergic agonists for regional anesthesia. A clinical review of clonidine. Anesthesiology. 1996;85:655-74.
8. Jacob A. K., Kopp S. L., Bacon D. R., Smith H. M.The History of Anesthesia. In: Barash PG, Cullin BF, Stoelting RK, eds. Clinical Anaesthesia, 6th ed. Philadelphia: Lippincott Williams and Wilkins 2009; p: 3-26.
9. Larson MD. History of anaesthetic practice. In Miller's anaesthesia. Ed by Ronald D Miller. 6th ed. Churchill Livingstone 2005; p: 3-52.
10. Brown D. L., Raymond B. History of anesthesia. In: Michael J. Cousins, Phillip O. Bridenbaugh, Daniel B. Carr, and Terese T. Horlocker, editors. Neural Blockade in Clinical Anesthesia and Pain Medicine, 4rth ed. Philadelphia: Lippincott Williams & Wilkins 2009; p: 1-5.

Conflict of Interest: Nil Source of support: Nil