

## **Intravenous Magnesium Sulphate for Postoperative Analgesia after Abdominal Hysterectomy under Spinal Anaesthesia with 0.5% Heavy Levobupivacaine**

<sup>1</sup>Dr.Raksha Sharma, Consultant Anaesthetist, Sudha Hospital, Kota, Rajasthan

<sup>2</sup>Dr.Ankur Dixit, Assistant Professor, Department of Anaesthesia, Sudha Medical College, Kota, Rajasthan

<sup>3</sup>Dr.Anshul Gautam, Senior Resident, Department of General Surgery, KKBM, Dehradun, Uttarakhand

<sup>4</sup>Dr.Ayushi Meena, Junior Resident, Department of Anaesthesia, Govt. Medical College, Kota, Rajasthan

**Corresponding Author:** Dr.Raksha Sharma, Consultant Anaesthetist, Sudha Hospital, Kota, Rajasthan

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**Conflicts of Interest:** Nil

### **Abstract**

**Objective:** Hysterectomy is the most common major gynaecological operation and is usually performed through laparotomy. Adequate analgesia that allows early mobilization with fewer complications is essential for improved postoperative recovery. The main objective of the present trial was to evaluate the effectiveness of magnesium sulphate as the study drug for postoperative analgesia in abdominal hysterectomy under spinal anaesthesia with 0.5% heavy levobupivacaine.

**Method:** This prospective clinical study was conducted on 80 adult patients aged 20-60 yrs, ASA grade I and II who were scheduled for abdominal hysterectomy. Patients were divided into two groups group S (study) and group C (control). Group S – Patients received magnesium sulphate 50mg/kg for 15 min. in 100ml NS after the spinal anaesthesia given with heavy levobupivacaine followed by 15mg/kg/hr intravenous magnesium sulphate infusion until the end of the surgery and group in C patients received spinal anaesthesia with heavy levobupivacaine. The time when first rescue

analgesia was given postoperatively and total rescue analgesia dosage required in first 24 hours were noted and compared in both the groups.

**Results:** The mean time of first rescue analgesia was 3.72 hours  $\pm$  0.81 in group S and in group C the mean time of first rescue analgesia 1.85 hours  $\pm$  0.80. Total mean analgesic required postoperatively within 24 hours postoperatively in group S was 218 mg  $\pm$  67.17 (standard deviation) and in group C 253.33 mg  $\pm$  52.41 (standard deviation).

**Conclusion:** Intraoperative administration of MgSO<sub>4</sub>(50 mg kg<sup>-1</sup> bolus followed by 15 mg kg<sup>-1</sup>h<sup>-1</sup> continuous infusion till the end of surgery) during total abdominal hysterectomy under spinal anaesthesia with levobupivacaine (heavy) reduced postoperative rescue analgesic requirement.

**Keywords:** IV Magnesium sulphate, Intrathecal levobupivacaine (0.5% H), Abdominal Hysterectomy, post op analgesia

## **Introduction**

Pain is the prime concern for most the patients undergoing surgeries despite development of newer generations of analgesic drugs, different strategies and interventions during perioperative period. Effective pain control may contribute to improved surgical outcomes, shorter hospital stays, and a decreased risk of developing chronic pain.<sup>1</sup>

Postoperative pain should be effectively treated because it represents an important component of postoperative recovery. Effective treatment serves to blunt autonomic, somatic and endocrine reflexes with a resultant potential decrease in perioperative morbidity. Opioids have been usually used as postoperative and intraoperative analgesic components, regardless of many adverse effects such as nausea, vomiting, respiratory depression and long-term effects like addiction, tolerance and dependence, opioid induced hyperalgesia (OIH), other pharmacological options can be non-steroidal anti-inflammatory drugs (NSAIDS), non-opioids and local anaesthetics, but none of the agents exclusively can be used without side effects to inhibit nociception.<sup>2-4</sup>

Hysterectomy is the most common major gynaecologic operation and is usually performed through laparotomy. Abdominal Hysterectomy is associated with an intense inflammatory response that can result in moderate to severe postoperative pain, sometimes difficult to control. Adequate analgesia that allows early mobilization with fewer complications is essential for improved postoperative recovery. Perioperative regional anaesthesia is often used in fast-track programs.<sup>5</sup>

The main objective of the present trial was to evaluate the effectiveness of magnesium sulphate as the study drug for postoperative analgesia in abdominal hysterectomy under spinal anaesthesia with heavy levobupivacaine. The parameters noted were duration of

analgesia, time of first rescue analgesia in postoperative period, time of occurrence of pain in postoperative period, total rescue analgesia requirement in 24 hours. Respiratory rate, pulse rate, blood pressure, urine output, SpO<sub>2</sub> were monitored perioperatively and compared with control group.

## **Methods**

The present study was carried out in the Department of Anaesthesiology and Critical Care, Government Medical College and Associated Groups of Hospitals, Kota. After hospital ethical committee's approval and written informed consent obtained from all patients, this prospective clinical study was conducted on 80 adult patients aged 20-60 yrs, ASA grade I and II who were scheduled for abdominal hysterectomy. Patient who refused to give consent, patient with history of any drug allergy, hemodynamically unstable patients or with severe morbidity were excluded from study.

### **Inclusion criteria**

- ASA grade I and II
- Patients with weight 30 kg to 70 kg
- Patient with age 20 – 60 yrs

### **Exclusion criteria**

- ASA grade III and IV
- Patient refusal
- History of coagulopathy, neuromuscular, cardiovascular, pulmonary, renal, hepatic, psychiatric disease.
- Patient with known hypersensitivity for levobupivacaine or magnesium sulphate.
- Patient with infection or ulceration at the place of spinal anaesthesia.

The patients were randomly allocated into two groups.

**Group Study (S)** – Patients received magnesium sulphate 50mg/kg for 15 min. in 100ml NS after the

spinal anaesthesia given with heavy levobupivacaine followed by 15mg/kg/hr intravenous magnesium sulphate infusion until the end of the surgery.

**Group Control (C)**– Patients received spinal anaesthesia with heavy levobupivacaine

#### Monitoring

- Heart rate
- Blood pressure (systolic, diastolic)
- SpO<sub>2</sub>(oxygen saturation)
- ECG
- Urine output
- Respiratory Rate

#### Procedure

After taking informed consent from the patients going for abdominal hysterectomy under spinal anaesthesia using hyperbaric levobupivacaine 0.5%, patients were divided into 2 groups (Group S and Group C). Pre anaesthetic evaluation was done before surgery. All patients were kept fasting overnight and pre-medicated with oral alprazolam 0.5mg and ranitidine 150 mg on night before surgery and in the morning of surgery. Both group patients were preloaded with ringer lactate at 10ml/kg. After taking preoperative vitals of patients, under all aseptic precautions with 25 G spinal needle (quincke) injection levobupivacaine (heavy) was given at L<sub>3</sub> - L<sub>4</sub> level after positive aspiration for spinal fluid with loss of resistance technique.

With the level of significance (alpha) = 0.05 and power of 80%, sample size required was 40 per group.

Group S (n=40) - patients were administered magnesium sulphate 50mg/kg intravenously in 100 ml NS for 15 minutes after giving spinal anaesthesia using levobupivacaine, followed by magnesium sulphate infusion of 15ml/hr till the end of surgery. Group C (n=40) – patients were administered the same amount of

normal saline after giving spinal anaesthesia with heavy levobupivacaine.

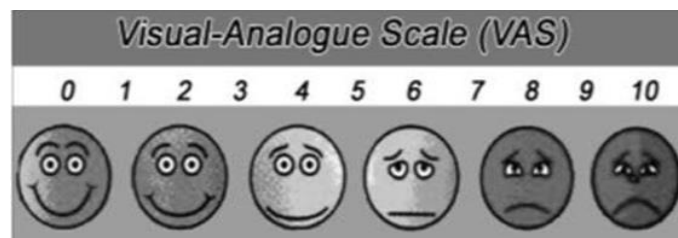
Throughout the surgery hemodynamic parameters like heart rate, blood pressure, SpO<sub>2</sub>, ECG, urine output was monitored.

After completion of the surgery all the patients were shifted to their respective post operative ward and the patients were counselled about the VAS score. Blood pressure, SpO<sub>2</sub>, respiratory rate and urine output were noted for 24 hours and compared between both the groups.

#### Rescue Analgesia

Rescue analgesia refers to additional analgesic given postoperatively when VAS becomes >3. All patients were observed for intensity of pain in post-operative period and were measured using a 10 cm Visual analogue scale (VAS) (where 0 = no pain and 10 = worst). The VAS was measured at 1, 2, 3, 4, 8, 12 and 24 hours respectively. The rescue analgesia was given by injection tramadol (2.5mg/kg i.v) sos with inj. Ondansetron 0.1mg/kg.

The time when first rescue analgesia was given postoperatively and total rescue analgesia dosage required in first 24 hours were noted and compared in both the groups.



**Observations and Results**

Table 1: Distribution of age, height and weight

Parameters	Group	Mean ± Standard Deviation	p-value
Age (years)	Group S	49.45 ± 8.4	0.3936
	Group C	49.92 ± 6.7	
Height (cms)	Group S	145.67 ± 5.72	0.09
	Group C	147.42 ± 4.77	
Weight(kgs) (mean ± SD)	Group S	63.25 ± 7.56	0.2912
	Group C	62.35 ± 6.92	

There was even distribution of age, height and weight in two groups. Table 1. showing age distribution, height distribution and weight distribution of the patients in both the groups. The mean age was 49.95 +/- 8.4 and 49.92 +/- 6.7 in group S and group C respectively. The mean height was 145.67 +/- 5.72 and 147.42 +/- 4.77 in group S and group C respectively. The mean weight was 63.25kgs ± 7.56 and 62.35kgs ± 6.92 in group T and group C respectively. There was no significant difference in the age, weight, height of patients between the two groups studied. Both groups were similar with respect to age distribution (P>0.05).

Figure 1: Mean age distribution group wise

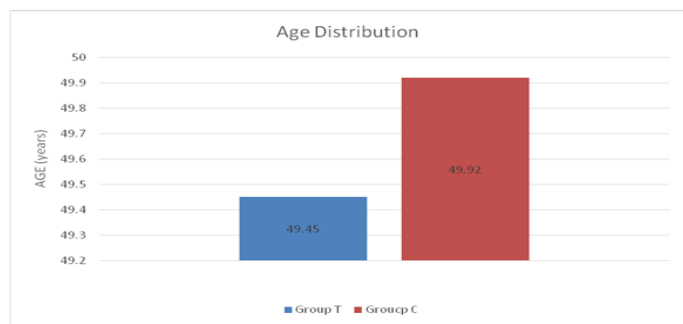


Figure 3: Mean Weight Distribution group wise.

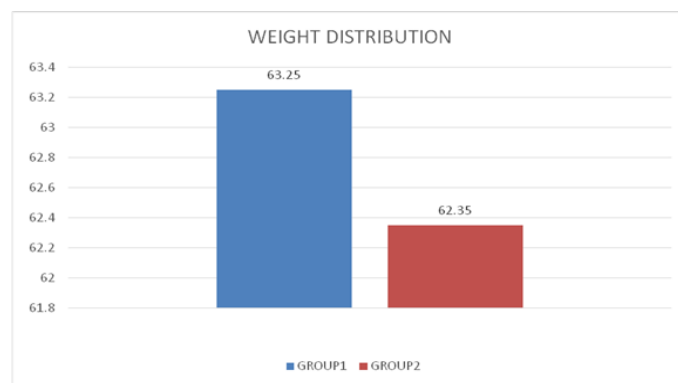


Figure 2: Mean Height Distribution group wise

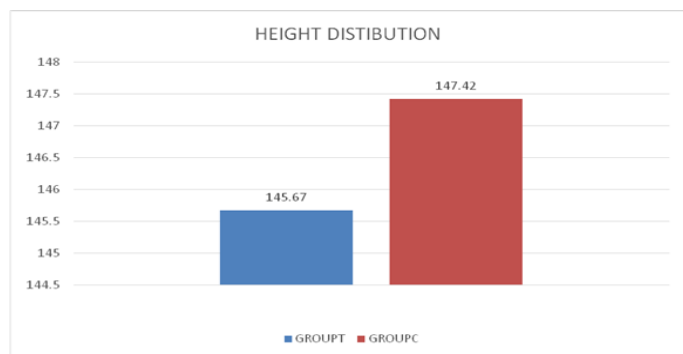


Table 2: Mean time of first rescue analgesia (hrs)

Parameter	GROUP S (Mean ± S.D.)	GROUP C (Mean ± S.D.)	p-value
Duration of Analgesia (In Hrs) (mean ± SD)	3.72 ± 0.81 (hrs ± S.D.)	1.85 ± 0.80 (hrs ± S.D.)	p<0.0001

Table 2 is showing comparison in mean time of first rescue analgesia in both groups studied. The mean duration of analgesia was  $3.72 \pm 0.81$  and  $1.85 \pm 0.80$  in group S and group C respectively. There is a significant difference in the duration of analgesia between the two groups studied. ( $P < 0.0001$ ).

Figure 4: Mean duration of analgesia group wise

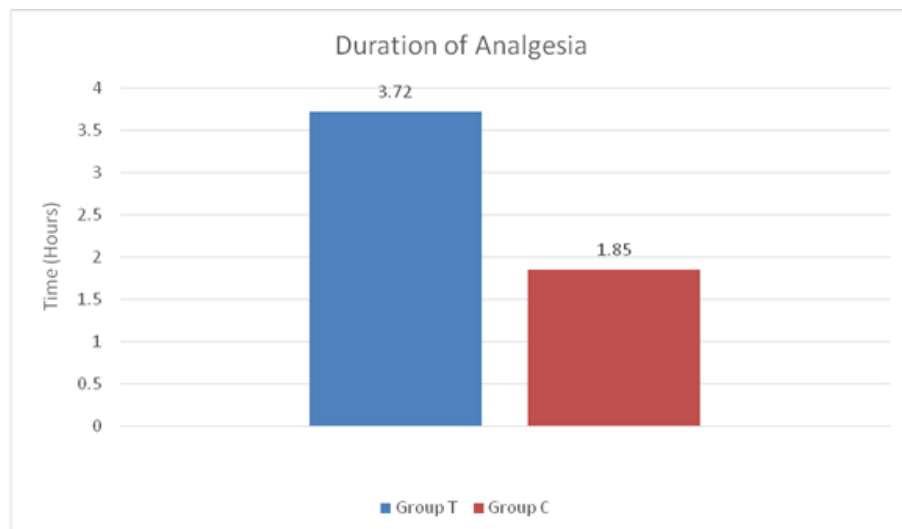


Table 3: Comparison of Postoperative Analgesia (In Terms Of Vas Score) Between the Groups at Various Time Intervals

Time interval in postop period	GROUP S (mean $\pm$ Standard deviation)	GROUP C (mean $\pm$ Standard deviation)	P Value
0hr	0	0	
1hr	$0.95 \pm 0.45$	$3.1 \pm 0.92$	$p < 0.0001$
2 hr	$1.6 \pm 0.74$	$3.27 \pm 1.37$	$p < 0.0001$
3 hrs	$2.8 \pm 1.22$	$2.82 \pm 1.35$	$p < 0.0001$
4 hrs	$3.1 \pm 0.98$	$2.15 \pm 1.05$	$p < 0.0001$
6 hrs	$2.5 \pm 0.67$	$2.4 \pm 1.05$	$P = 0.3085$
12hrs	$3.1 \pm 0.98$	$3.05 \pm 1.01$	$P = 0.4129$
18hrs	$1.62 \pm 0.66$	$1.8 \pm 0.68$	$P = 0.1151$
24hrs	$1.52 \pm 0.69$	$1.4 \pm 0.49$	$P = 0.1515$

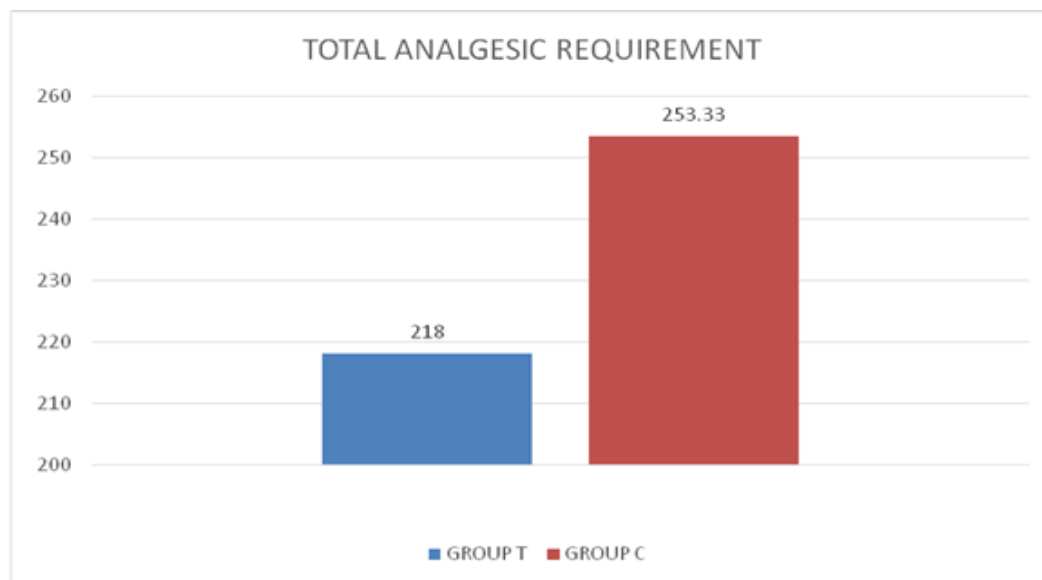
Table 3 shows comparison of mean postoperative analgesia in terms of VAS score in between the groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. There was a significant difference in VAS score at 1, 2, 3 and 4 hours postoperatively ( $p < 0.0001$ ), whereas there was no significant difference in VAS score 6, 12, 18, 24 hours postoperatively ( $p > 0.0001$ ).

Table 4: Total Mean Analgesic Required

Groups	Total Mean Analgesic Required Mean $\pm$ S.D.	P Value
Group S	218 mg $\pm$ 67.17	$P > 0.005$
Group C	253.33 mg $\pm$ 52.41	

Table number 4 Shows total mean analgesic required in both the groups within 24 hours postoperatively. There was a significant difference between total mean analgesic given in both the groups.

Figure 5:



### Postoperative Vitals

Table 5: Comparison of Mean Pulse Rate (Beats Per Minute) Between The Groups at Various Time Intervals

PR At Various Time Intervals	Group S (beats per minute) mean $\pm$ S.D.	Group C (beats per minute) mean $\pm$ S.D.	P Value
0 hr	75.325 $\pm$ 9.869371	76.575 $\pm$ 6.597931	0.125
1 hr	73.8 $\pm$ 9.626885	74.475 $\pm$ 7.828244	0.122
2 hr	73.225 $\pm$ 9.825366	78.675 $\pm$ 7.923958	0.062
3 hrs	76.8 $\pm$ 10.5956	78.45 $\pm$ 6.972289	0.251
4 hrs	77.4 $\pm$ 9.644448	76.575 $\pm$ 7.503461	0.0625
6 hrs	78.3 $\pm$ 9.101141095	80.625 $\pm$ 7.095277	0.0125
12 hrs	79.3 $\pm$ 9.554701	77.175 $\pm$ 7.139229	0.135
18 hrs	73.275 $\pm$ 8.747124	74.775 $\pm$ 6.881739	0.192
24 hrs	72.625 $\pm$ 8.900266	74.975 $\pm$ 6.573012	0.258

Table 5 shows comparison of mean pulse rate in between both groups at 0, 1, 2, 3, 4, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean pulse rate between both the groups except at 6 hours postoperatively.

Figure 6: Mean Pulse Rate at different time interval group wise

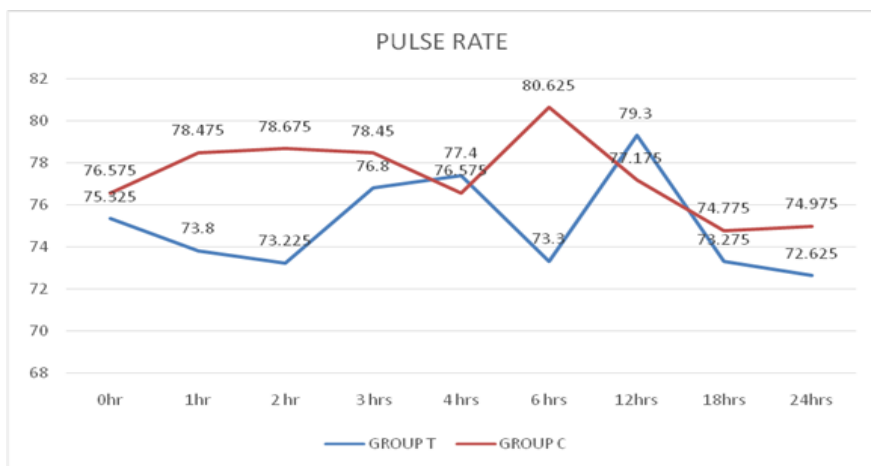


Table 6: Comparison of Mean Respiratory Rate between The Groups

TIME	GROUP S (breaths per minute) Mean ± S.D.	GROUP C (breaths per minute) Mean ±S.D.	P Value
0hr	13.625±0.776250026	13.15±0.83359	0.19
1hr	12.875±0.952392	12.85±0.662164	0.441
2 hr	13.075±0.852974	12.875±0.647975	0.140
3 hrs	12.925±0.971055	12.575±0.747217	0.065
4 hrs	12.85±0.828576	12.875±0.647975	0.446
6 hrs	12.875±0.975337	13.025±0.76753	0.209
12hrs	12.975±0.882523	13.025±0.530481	0.392
18hrs	12.85±1.025008	12.725±0.715667	0.322
24hrs	12.75±0.863801972	12.875±0.757441713	0.458

Table 6 shows comparison of mean respiratory rate in between both groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean respiratory rate between both the groups. (P>0.05).

Figure 7: Mean respiratory rate at different time intervals group wise

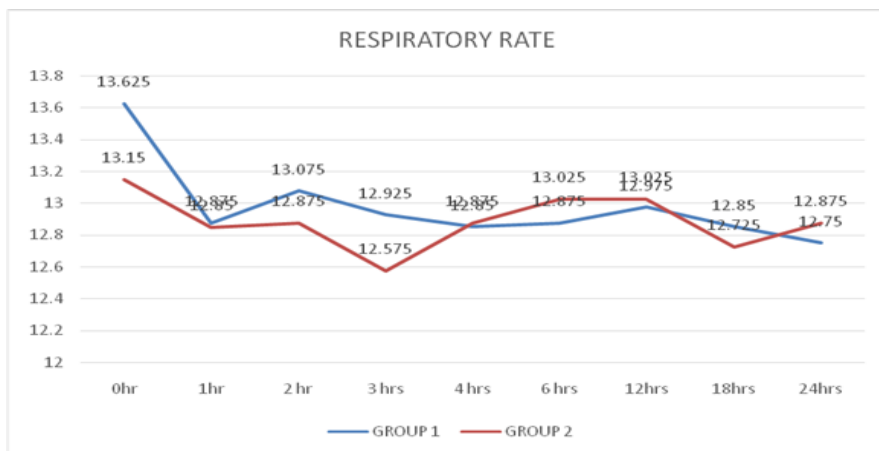


Table 7: Comparison of Mean Spo2 between The Groups

TIME	GROUP S Mean ± S.D.	GROUP C Mean ± S.D.	p VALUE
0hr	99.35±0.76961	99.7±0.516398	0.325
1hr	99.325±0.76418215	99.9±0.378932	0.266
2 hr	99.025±0.69752309	99.825±0.384808	0.369
3 hrs	99.3±0.516397779	99.875±0.334932	0.452
4 hrs	99.05±0.597001052	99.675±0.729858	0.425
6 hrs	99.975±0.158114	99.975±0.158114	0.500
12hrs	99.85±0.36162	99.85±0.36162	0.500
18hrs	99.95±0.220721	99.95±0.220721	0.500

Table 7 shows comparison of SpO<sub>2</sub> in between both groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean SpO<sub>2</sub> between both the groups. (P>0.05).

Figure 8: Mean SpO<sub>2</sub> at different time intervals group wise

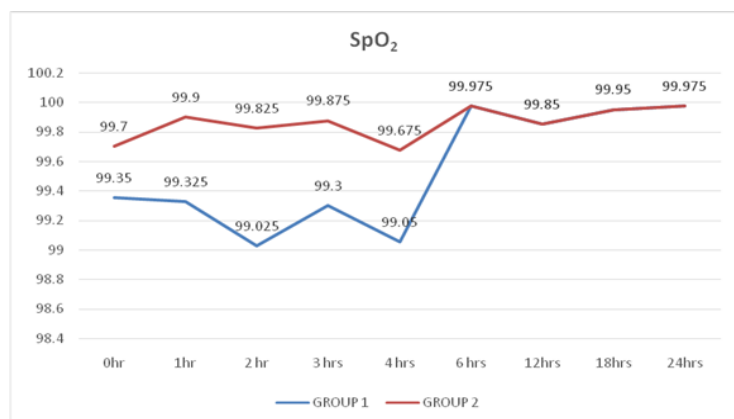


Table 8: Comparison of Mean Systolic Blood Pressure between The Groups

TIME	GROUP S (mmhg) Mean ± S.D.	GROUP C (mmhg) Mean ± S.D.	P Value
0hr	124.25 ±7.807787	125.8 ± 5.743223	0.325
1hr	126.25 ±4.902903	119.3± 7.693487	0.112
2 hr	120.75 ±7.298577	126.25± 5.568916	0.064
3 hrs	124±4.961389	121.8± 9.089865	0.125
4 hrs	129.75± 1.581139	127.6±4.667399	0.351
6 hrs	125 ±5.063697	125.7±5.862528	0.0622
12hrs	125 ± 5.063697	125.65±5.356759	0.499
18hrs	123.25± 4.743416	120.9±4.049691	0.125
24hrs	125±5.063697	126.4±1.822931	0.251

Table 8 shows comparison of systolic blood pressure in between both the groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean systolic blood pressure between both the groups. (P>0.05).

Figure 9: Mean Systolic BP at different time intervals group wise

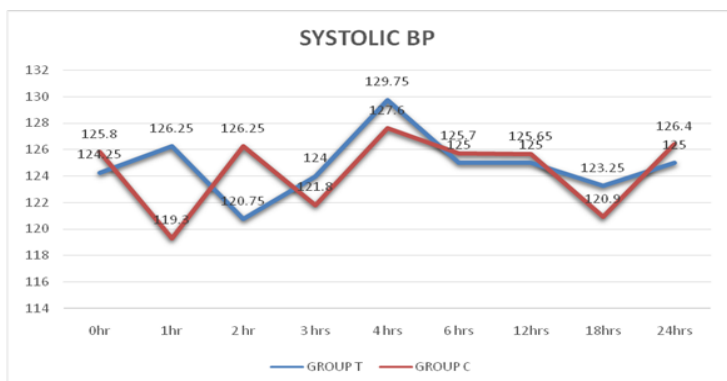
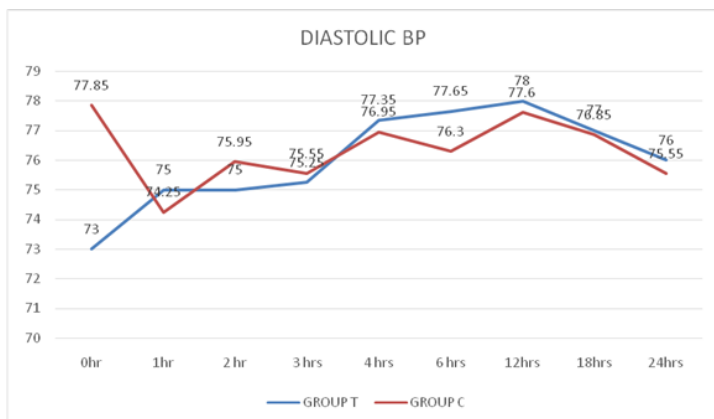


Table 9: Comparison of mean Diastolic Blood Pressure Between the Groups

TIME	GROUP S (mmhg) Mean ± S.D.	GROUP C (mmhg) Mean ± S.D.	P-Value
0hr	73±4.640955	77.85±4.693421	0.250
1hr	75±4.640955	74.25±4.155626	0.0525
2 hr	75±5.063697	75.95±5.25235	0.452
3 hrs	75.25±5.057363	75.55±4.803578	0.500
4 hrs	77.35±4.927942	76.95±5.406312	0.062
6 hrs	77.65±3.945462	76.3±4.783519	0.082
12hrs	78±4.050957	77.6±4.754485	0.125
18hrs	77±4.640955	76.85±5.250397	0.255
24hrs	76±4.961389	75.55±4.950783	0.266

Table 9 shows comparison of diastolic blood pressure in between both the groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean diastolic blood pressure between both the groups. (P>0.05).

Figure 10: Mean Diastolic BP at different time intervals group wise



## Discussion

Generally, opioids are used in every patient for post-operative analgesia which has its own side effects like nausea, vomiting, respiratory depression and long-term effects like addiction, tolerance and dependence, opioid induced hyperalgesia (OIH). Benyamin R, Trescot AM, Datta S et al<sup>2</sup> (2008) wrote a paper on opioid complications and side effects. They mentioned common side effects of opioid administration include sedation, dizziness, nausea, vomiting, constipation, physical dependence, tolerance, and respiratory depression. Physical dependence and addiction are clinical concerns that may prevent proper prescription and in turn inadequate pain management.

To reduce the dependency on opioids different studies are done to test different methods of pre-emptive analgesia.<sup>6-7</sup> Similarly action of intravenous magnesium sulphate was observed under our study titled “Intravenous Magnesium Sulphate For Postoperative Analgesia After Abdominal Hysterectomy Under Spinal Anaesthesia With Heavy Levobupivacaine”

In our study we evaluated the effectiveness of magnesium sulphate as the postoperative analgesic in abdominal hysterectomy under spinal anaesthesia with heavy levobupivacaine by monitoring-

- Hemodynamic changes in terms of heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure
- Time of first rescue analgesia
- Total rescue analgesic requirement in 24 hours.

## Demographic distribution

There was an even distribution of age, weight and height in the two groups. As evident from table number 1, the mean age was 49.95 +/- 8.4 and 49.92 +/- 6.7 in group S and group C respectively. There was no significant difference in the age of patients between the two groups

studied. The mean height was 145.67 +/- 5.72 and 147.42 +/- 4.77 in group S and group C respectively. There was no significant difference in the height of patients between the two groups. The mean weight was 63.25kgs ± 7.56 and 62.35kgs ± 6.92 in group S and group C respectively. There was no significant difference in the weight of patients between the two groups studied.

After the procedure, all patients were observed 24 hours postoperatively. Time of first rescue analgesia and total rescue analgesic requirement in 24 hours was noted and compared between both the groups. Hemodynamic changes in terms of heart rate, respiratory rate, systolic blood pressure, diastolic blood pressure and mean arterial pressure were noted and compared between both the groups upto 24 hours postoperatively.

## Time of First Rescue Analgesia (when VAS >3) -

In group S the mean time of first rescue analgesia was 3.72 hours ± 0.81 (standard deviation) and in group C the mean time of first rescue analgesia 1.85 hours ± 0.80 (standard deviation). There was a significant difference between both the groups' time of first rescue analgesia  $P < 0.0001$ .

Similarly, Yamini Dhengle, Prerana N. Shah et al<sup>8</sup> did a research paper in 2016 where they studied effect of magnesium sulphate in for postop analgesia undergoing lower abdominal surgeries and lower limb surgeries.

## Total Mean Analgesic Requirement-

Total mean analgesic required postoperatively within 24 hours postoperatively in group S was 218 mg ± 67.17 (standard deviation) and in group C 253.33 mg ± 52.41 (standard deviation). There was a significant difference between both the groups' total mean analgesic requirement within 24 hours postoperatively.  $P < 0.0001$ .

Our findings were similar to the study conducted by H-J Shin, E.-Y. Kim<sup>9</sup> in 2016 in South Korea where they studied the effect of magnesium sulphate for

postoperative pain in patients undergoing bilateral total knee arthroplasty. In the control group, the amount of rescue analgesics (ketoprofen) used during the first 24h post-surgery was significantly higher. Magnesium significantly reduced the amounts of rescue analgesics administered over the first 24 h postoperatively. Rescue analgesia ketoprofen used in control group was 25 mg and in test group was 7 mg.

The following hemodynamic parameters were noted upto 24 hours postoperatively and compared between both the groups-

- Heart rate (beats per minute)
- Respiratory rate (breadths per minute)
- Systolic blood pressure (mmhg)
- Diastolic blood pressure (mmhg)
- Oxygen saturation (SpO<sub>2</sub>)

#### **Heart Rate**

As table 5 shows comparison of mean pulse rate in between both groups at 0, 1, 2, 3, 4, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean pulse rate between both the groups except at 6 hours postoperatively.

Our findings similar to Yamini Dhengle, Prerana N. Shah<sup>8</sup> research paper where she found that there was no significant difference in the mean pulse rate between both the groups.

#### **Respiratory Rate**

As table 6 shows comparison of mean respiratory rate in between both groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean respiratory rate between both the groups.

#### **Oxygen Saturation**

As Table 7 shows comparison of SpO<sub>2</sub> in between both groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant

difference in the mean SpO<sub>2</sub> between both the groups. (P>0.05).

#### **Systolic Blood Pressure**

As table 8 shows comparison of systolic blood pressure in between both the groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean systolic blood pressure between both the groups. (P>0.05).

#### **Diastolic Blood Pressure**

As table 9 shows comparison of diastolic blood pressure in between both the groups at 0, 1, 2, 3, 4, 6, 12, 18 and 24 hours postoperatively. On comparison there was no significant difference in the mean diastolic blood pressure between both the groups. (P>0.05).

Our observations noted for hemodynamic parameters were similar to the study done by Yamini Dhengle, Prerana N. Shah etal (2016)<sup>8</sup> and Kara H, Sahin N, Uluhan etal<sup>10</sup> (2002) who observed that there was no significant difference between hemodynamic parameters of study group and control group post-operatively.

#### **Results**

- The mean time of first rescue analgesia was 3.72 hours ± 0.81 in group S and in group C the mean time of first rescue analgesia 1.85 hours ± 0.80 .
- Total mean analgesic required postoperatively within 24 hours postoperatively in group S was 218 mg ± 67.17 (standard deviation) and in group C 253.33 mg ± 52.41 (standard deviation).

So, we conclude that intraoperative administration of MgSO<sub>4</sub> (50 mg kg<sup>-1</sup>boluses followed by 15 mg kg<sup>-1</sup>h<sup>-1</sup> continuous infusions till the end of surgery) during total abdominal hysterectomy under spinal anesthesia with levobupivacaine (heavy) reduced postoperative rescue analgesic requirement. It improved postoperative analgesia by delaying as well as decreasing the need of postoperative analgesic. There was no

significant difference in hemodynamic variables and sedation in both groups.

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