ORIGINAL ARTICLE ASIAN JOURNAL OF MEDICAL SCIENCES

Comparison of the effect of intrathecal fentanyl citrate and magnesium sulfate as adjuvants to hyperbaric levobupivacaine 0.5% for spinal anesthesia in patients undergoing lower limb orthopedic surgeries

Anusha Tripathy[1], Neelima Tandon[2], Namrata Jain[3], Devendra Singh[4]

[1,4]Postgraduate Resident, Department of Anesthesiology, Gajra Raja Medical College and J. A. Group of Hospital, [2]Professor and Head, [3]Assistant Professor, Department of Anesthesiology, Super Speciality Hospital, Gajra Raja Medical College and J. A. Group of Hospital, Gwalior, Madhya Pradesh, India

Submission: 17-05-2024 Revision: 20-07-2024 Publication: 01-09-2024

ABSTRACT

Background: Subarachnoid blockade is a safe, reliable, and inexpensive technique that provides surgical anesthesia along with prolonged post-operative analgesia. The quality of subarachnoid block is enhanced by the addition of intrathecal adjuvants, such as fentanyl citrate and magnesium sulfate to hyperbaric levobupivacaine. **Aims and Objectives:** The aim of this study was to compare the effects of fentanyl and magnesium sulfate as adjuvants to 0.5% hyperbaric levobupivacaine in orthopedic surgeries under subarachnoid block. **Materials and Methods:** This prospective randomized study included 90 American Society of Anesthesiologists Grade I and II patients aged 18–60 years undergoing orthopedic surgeries. Group LS received 3 mL 0.5% levobupivacaine heavy + 0.5 mL normal saline. Group LF received 3 mL 0.5% levobupivacaine heavy + fentanyl 25 µg, and Group LM, 3 mL 0.5% levobupivacaine heavy + magnesium sulphate 50 mg + 0.4 mL normal saline. The onset and duration of sensory and motor block and intraoperative hemodynamics were recorded. In the post-operative period, duration of analgesia, Visual Analog Scales scores, and side effects were observed. **Results:** The onset of sensory block was 4.04 ± 0.74 min in Group LM ($P < 0.001$) as compared to Groups LF (2.01 ± 0.23 min) and LS (2 ± 0.24 min). The onset of motor blockade took 5 ± 1.14 min in the control group, 7.01 ± 0.94 in group LF, and 8.11 ± 1.33 min in group LM ($P < 0.001$). The duration of analgesia in group LS was 183.73 ± 12.08 min, 317 ± 18.6 min in group LF, and 219.43 ± 20.89 in group LM ($P < 0.001$). **Conclusion:** The addition of fentanyl and magnesium as adjuvants enhanced the quality of subarachnoid block when added to hyperbaric levobupivacaine. The duration of analgesia was longest in fentanyl, followed by magnesium and then control. The incidence of side effects was greatest in fentanyl, followed by control and nil in magnesium.

Key words: Levobupivacaine; Hyperbaric; Fentanyl; Magnesium; Subarachnoid block

Access this article online

Website: http://nepjol.info/index.php/AJMS

DOI: 10.3126/ajms.v15i9.65936

E-ISSN: 2091-0576

P-ISSN: 2467-9100

Copyright (c) 2024 Asian Journal of Medical Sciences

This work is licensed under a Creative Commons Attribution-NonCommercial 4.0 International License.

INTRODUCTION

Most lower limb orthopedic surgeries can be safely undertaken with regional anesthesia in the form of the subarachnoid block. This technique was first undertaken by Bier with the administration of cocaine in 1898.[1]

Over the decades, local anesthetics have developed into an entire class of drugs, the most recent of which is levobupivacaine,[2] which stands to dethrone its predecessor, bupivacaine, by the decreased incidence of cardiovascular toxicity.[3] Levobupivacaine is an amide local anesthetic, a pure S (-) enantiomer of bupivacaine free from its neural and

Address for Correspondence:
Dr. Devendra Singh, Postgraduate Resident, Department of Anaesthesiology, Gajra Raja Medical College and J. A. Group of Hospital, Gwalior, Madhya Pradesh, India. **Mobile:** +91-7049901951. **E-mail:** daredevilldev@gmail.com

cardiovascular side effects due to a lower free drug to protein-bound ratio.[4] The hyperbaric formulation is faster acting in the onset and recovery of sensory and motor blockade.[5]

The addition of adjuvants to improve the quality, duration, and side effect profile of subarachnoid block is a much researched on subject. Fentanyl is a synthetic opioid, which produces rapid onset of analgesia following intrathecal administration due to its lipophilicity.[6] The addition of intrathecal fentanyl to spinal anesthesia has been seen to prolong sensory blockade without prolonging motor recovery.[7]

N-methyl-D-aspartate (NMDA) receptor activity has been associated with central hypersensitivity to pain. Magnesium is an NMDA antagonist that has been described to induce a reduction in central sensitization from peripheral pain stimuli, thereby leading to preemptive analgesia.[8]

In our database search, we came across limited published studies on the combination of hyperbaric levobupivacaine+fentanyl or magnesium. Therefore, in this prospective randomized controlled study, we have compared the intrathecal addition of 50 mg magnesium sulfate and 25 mcg fentanyl citrate as adjuvants to 3 mL 0.5% levobupivacaine heavy in spinal anesthesia for lower limb orthopedic surgeries.

Aim

To evaluate the duration of analgesia of levobupivacaine heavy with magnesium sulfate or fentanyl citrate compared to control (normal saline).

Objectives

1. To determine and compare the time of onset and duration of sensory blockade of fentanyl and magnesium when added to 0.5% levobupivacaine heavy intrathecally
2. To determine and compare the time of onset and duration of motor blockade of fentanyl and magnesium when added to 0.5% levobupivacaine heavy intrathecally
3. To determine the hemodynamic profile of both drugs
4. Incidence of side effects, if any.

MATERIALS AND METHODS

This prospective randomized double-blind study was undertaken after the clearance of our institutional ethics committee on patients consenting to participate in the study, aged between 18 and 60 years, of the American Society of Anesthesiologists (ASA) Grade I or II, admitted to undergo lower limb orthopedic procedures in our institute; while patients declining consent, aged <18 or >60, ASA Grades III or IV, suffering from any respiratory, cardiac, hepatic, renal, neurological, or coagulation disorder, already receiving opioid or magnesium therapy, or having any local infection at the site of injection of spinal anesthesia, were excluded from the study.

The average time for onset of sensory block was taken as 5 min with a standard deviation 1 min in Levobupivacaine+Fentanyl group[9,10] and 6 min with a standard deviation 1 min in Levobupivacaine+Magnesium sulphate[11] at 95% confidence interval and 95% power of test, using the formula:

$$n = (S_1^2 + S_2^2)(Z_{(\alpha/2)} + Z_{(1-\beta)})2 / (\mu_1 - \mu_2)^2$$

Where S_1=1 min, =1 min

μ= 5 min, μ= 6 min

$Z_{\infty/2}$=1.96, $Z_{1-\beta}$=1.64

Substituting these values into the formula, we obtained n=26, which we approximated to 30.

Hence, 30 patients were allotted to each group.

The groups were divided as follows: Group LS (n=30): 3 mL of 0.5% levobupivacaine heavy+0.5 mL of normal saline; Group LF (n=30): 3 mL of 0.5% levobupivacaine heavy+0.5 mL of fentanyl (25 μg); Group LM (n=30): 3 mL of 0.5% levobupivacaine heavy+0.1 mL of 50% magnesium sulfate (50 mg)+0.4 mL normal saline. Randomization was done by the sealed envelope method. Both the investigator and the patient were blinded to the composition of the study drug chosen for the particular patient, which was prepared by an independent anesthesiologist not involved in the injection of the drug or monitoring of the patient parameters.

We examined the patient a day before surgery for a complete general, physical, and systemic examination. We conducted the required routine investigations including complete blood count, random blood sugar, blood urea, serum creatinine, electrocardiography, and chest radiography. We explained the purpose and protocol of the study to the patient and thereafter, informed written consent was obtained. The patient was kept nil orally for at least 6 h before the procedure. On arrival of the patient in the operation theater, the procedure was explained in detail. Intravenous access with 18G cannula was obtained in the patient's forearm for preloading with Ringer's lactate (10 mL/kg), and routine monitors recorded the patient's baseline vital parameters, including heart rate (HR), non-invasive systolic blood pressure (SBP), diastolic blood pressure

(DBP) and mean arterial blood pressure (MAP), and SpO_2 preoperatively.

Under all aseptic precautions, the patient was kept in a sitting position, while a lumbar puncture was done at the L3-L4 intervertebral space via midline approach with a 25G Quincke spinal needle. After ensuring free flow of cerebrospinal fluid, the study drug was injected and the patient kept in supine position for the remainder of the study period. During surgery, any fall in MAP below 20% of baseline value was treated with injection Mephentermine 6 mg i.v. and a fall in HR <60 beats/min was treated with injection Atropine sulfate 0.3–0.6 mg i.v. and recorded.

The block characteristics were observed in terms of time for onset of sensory block (upto T10) and motor block (Bromage 3), duration of sensory block (regression to S1) and motor block (Bromage 0), duration of analgesia (Visual Analog Scales [VAS] score >3) and time for first rescue analgesia. The hemodynamic parameters such as blood pressure and HR were observed and recorded at 3 min, 5 min, 10 min, 15 min, 30 min, 60 min, 90 min, 120 min, and 150 min after the injection of the study drug, and compared among all three study groups. Post-operative hourly VAS scores and the incidence of side effects were noted. Injection Tramadol 100 mg in 100 mL normal saline was administered when patients reported a VAS score >3.

The observations recorded in the three groups were tabulated and statistical analysis was carried out using a statistical software Statistical Package for the Social Sciences 20.0. The Chi-square test, one-way ANOVA, and Tukey *post hoc* test were used wherever the appropriate statistical test was required. P<0.05 was taken as statistically significant.

RESULTS

The demographic data of both the groups were comparable in respect to age in years and sex. The difference between the study groups were not statistically significant (p > 0.05) (Table 1). Time for onset of sensory block (min) was significantly delayed in magnesium group. Time for onset of motor block was significantly different among all three groups. Duration of sensory as well as motor block was less in group LM as compared to group LF. Both adjuvants prolonged the duration as compared to the saline group.). Mean duration of surgery showed statistically insignificant difference. (Table 2). Duration of analgesia was significantly less in group LS as compared to LM and group LF was significantly greater than both (Figure 1). On intergroup comparison of haemodynamic parameters (PR, SBP, DBP and MAP) of Groups LF, LM and LS, we observed statistically insignificant difference throughout all of the time intervals (Figures 2 and 3).

In our study the incidence of side effects was more frequent in group LF as compared to group LS, and nil in group LM (Table 4).

DISCUSSION

Hyperbaric levobupivacaine can be used to provide surgical anesthesia for lower limb surgeries under subarachnoid block. We compared the addition of fentanyl citrate and magnesium sulfate as adjuvants to the local anesthetic drug.

All study participants belonged to ASA Grade I and II in our study in all the groups and hence, as shown in Table 1, the demographic characteristics were statistically insignificant and comparable among all three groups. The demographic characteristics were also comparable in studies conducted by Khezri et al.,[8] and Hemalatha et al.[11]

The time to sensory block onset until T10 did not significantly differ from each other in the fentanyl and control groups. However, magnesium delayed the onset of sensory block (P<0.001, Table 2). A similar study conducted by Khezri et al.,[8] also showed delayed onset in sensory and motor blockade in the magnesium group. Their explanation was that magnesium may have enhanced the metabolism of bupivacaine by cytochrome enzymes thereby delaying the onset of motor block. Khalili et al.,[12] conducted a similar study and also found that adding magnesium sulfate significantly delayed the onset of sensory blockade.

All three groups differed highly significantly from one another in terms of onset of motor blockade until Bromage Score 3 by one-way ANOVA and Tukey *post hoc* test as per Table 2. Our findings were in accordance with those observed by Gupta et al.,[13] and Khezri et al.,[8] who both had compared the effects of fentanyl and magnesium as adjuvants to hyperbaric bupivacaine in patients and Khalili et al.,[12] who compared magnesium+bupivacaine to a control. All these studies concluded that the addition of magnesium sulfate significantly prolonged the onset of sensory and motor blockade. Özalevli et al.,[14] added magnesium to fentanyl and isobaric bupivacaine and observed a delay in the onset of motor blockade in the study group as compared to control. The study explained that the delay in onset was possibly due to the change in the pH of the solution.

The duration of sensory block (Table 2) was shortest in control group LS, followed by group LM, and longest in LF (P<0.01). The addition of fentanyl prolonged the duration of a sensory block as compared to magnesium. The addition of fentanyl also prolonged the duration of the motor block as compared to magnesium which was

Table 1: Demographical distribution of the study population

Demographic characteristics	Group LS	Group LF	Group LM	P-value
Age (years) (Mean±SD)	39.1±12.91	36.97±13.02	38.47±11.19	0.75*
Sex distribution	Male=26 (86.67%) Female=4 (13.33%)	Male=19 (63.33%) Female=11 (36.67%)	Male=23 (76.67%) Female=7 (23.33%)	0.11**

P>0.05: Not significant, (*) One-way ANOVA applied, (**) Chi-square applied, SD: Standard deviation

Table 2: Sensory and Motor block characteristics compared among all three study groups

Block characteristics	Group LS (Mean±SD)	Group LF (Mean±SD)	Group LM (Mean±SD)	P-value (One-way ANOVA)
Onset of sensory block (min)	$2±0.24^{A}$	$2.01±0.23^{B}$	$4.04±0.74^{A,B}$	<0.001
Onset of motor block (min)	$5±1.14^{A,B}$	$7.01±0.94^{AA,C}$	$8.11±1.33^{C,B}$	<0.001
Duration of sensory block (min)	$140.13±7.35^{A,B}$	$241.73±22.74^{A,C}$	$188.27±22.88^{C,B}$	<0.01
Duration of motor block (min)	$112.23±7.29^{A,B}$	$212.37±20.4^{A,C}$	$145.6±37.31^{C,B}$	<0.001
Duration of surgery (min)	115.33±10.74	121.33±34.91	129.33±36.95	>0.05

One-way ANOVA applied and the same superscripts are significantly different (P<0.05) by Tukey *post hoc* test. P>0.05: Not significant, P<0.01: Statistically significant, P<0.001: Statistically highly significant, SD: Standard deviation

greater than the control (P<0.001) Similar results were found in the study conducted by Katiyar et al.,[15] comparing different doses of magnesium sulfate and fentanyl as adjuvants to bupivacaine for infraumbilical surgeries under subarachnoid block. They concluded that addition of fentanyl 25 μg showed a greater duration of sensory and motor block than magnesium 100 mg and 50 mg when added to bupivacaine for infraumbilical surgeries. Another study was done by Raghu et al.,[16] who found similar results in terms of duration of sensory and motor block, which was more when fentanyl 25 μg was added to bupivacaine heavy.

The results were controversial in the study by Khezri et al.,[8] who concluded that the duration of sensory and motor blockade was more in patients who received fentanyl with bupivacaine undergoing lower limb orthopaedic surgery due to its supraspinal effect while the duration of sensory and motor blockade in the magnesium group did not differ significantly from the control in their study. They stated that $MgSO_4$ might have activated the hydroxylation of bupivacaine by the CYP450 cytochromosomal enzyme and therefore, the addition of intrathecal $MgSO_4$ to spinal bupivacaine may have caused rapid elimination of bupivacaine. Similar to the above study by Khezri et al., and differing from ours, Unlugenc et al.,[17] observed that the addition of magnesium sulfate (50 mg) intrathecally to 10 mg of spinal bupivacaine (0.5%) did not prolong the duration of the sensory or motor blockade as compared to saline, while fentanyl did prolong the duration (P<0.05). Thus, magnesium sulfate may have altered bupivacaine pharmacokinetics in its intrathecal combination.

Various hemodynamic parameters such as HR, SBP, DBP, MAP, and SpO_2 were analyzed perioperatively at 0 min, 5 min, 10 min, 15 min, 30 min, 60 min, 90 min, 120 min, and

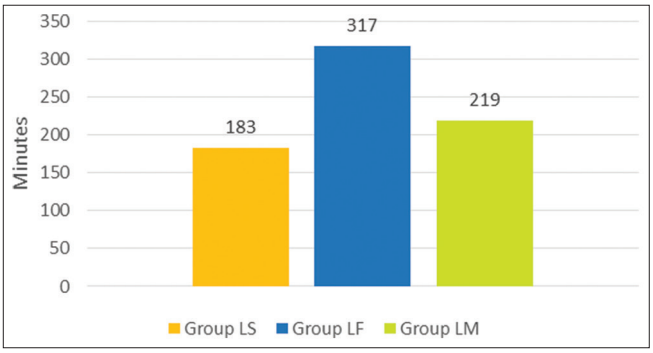

Figure 1: The comparison of the duration of analgesia among all three study groups in minutes. One-way ANOVA and Tukey *post hoc* test applied. P<0.05: statistically significant

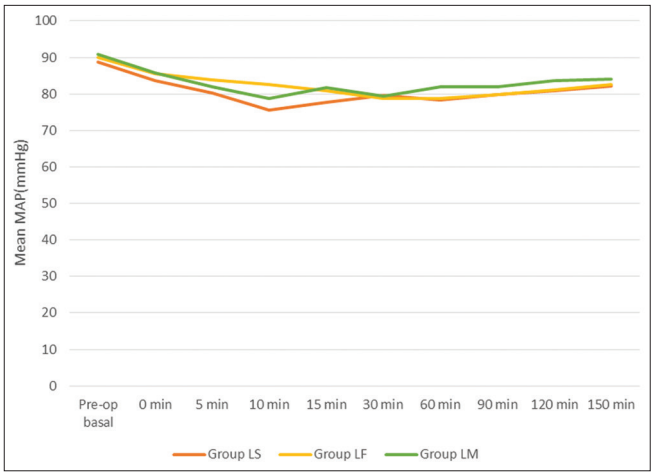

Figure 2: Intraoperative mean arterial blood pressure variation among all three groups (P>0.05)

150 min. PR, SBP, DBP, and MAP showed no statistically significant difference among the groups (P>0.05 at each interval). Our findings are in accordance with Gupta et al.,[13] who also observed a statistically insignificant difference between their fentanyl and magnesium groups.

Table 3: Comparison of post-operative VAS score

Time in hours	Group LS (Mean±SD)	Group LF (Mean±SD)	Group LM (Mean±SD)	P-value
1	0	0	0	
2	1.63±0.37	0	0	<0.01*
3	3.93±0.25	0.77±0.43	2.9±0.92	<0.01*
4		1.7±0.47	3.03±1.33	<0.01**
5		2.67±0.76		
6		3.57±1.01		

(*) One-way ANOVA test applied, (**) Chi-square test applied, P<0.01: Statistically significant, SD: Standard deviation

Table 4: Comparison of side effects among all three study groups

Side effect	Group LS	Group LF	Group LM
Nausea and vomiting	3	4	0
Respiratory depression	0	2	0
Dyspnoea	0	0	0
Hypotension	2	0	0
Pruritus	0	3	0
Bradycardia	0	2	0
Dysrrythmia	0	0	0
Shivering	4	2	0

Figure 3: Intraoperative mean heart rate variation among all three groups (P>0.05)

The duration of analgesia, shown in Figure 1, in group LS was 183.73±12.08 min, whereas it was 317±18.6 min and 219.43±20.89 min for LF and LM groups respectively. Hence, we see that the duration of analgesia was greatest in group LF, followed by group LM, and least in group LS. Table 3 shows the comparison of post-operative VAS scores. VAS score was greater in group LS as compared to group LF and LM, showing inadequate pain control in the control group, as compared to magnesium and fentanyl. VAS score >3 was managed with the administration of rescue analgesia to relieve post-operative pain. Thus due to fentanyl improving the duration and quality of analgesia better compared to magnesium, patients in LF group had lower VAS scores throughout the observation period and the administration of rescue analgesia was also delayed in group LF as compared to groups LS and LM. Similar findings were seen in the study done by Raghu et al.,[16] The mean post-operative VAS score at 2 h after surgery was 1.04±0.19 in Group F and 1.18±0.4 in Group M. Similarly, at 6, 12, and 24 h after surgery, the VAS score was less in Group F as compared to Group M. Our results are in accordance with the study conducted by Khezri et al.,[8] in which time to first request of analgesic in patients undergoing lower limb orthopedic surgeries under spinal anesthesia was more in the fentanyl group at 699.375±79.80 min, whereas patients who received magnesium had early time to first request of analgesic at 318.33±74.62 min. The expected reason for superior analgesia in group LF is thought to be fentanyl demonstrating a supraspinal effect by its cephalic spread and binding to opioid receptors.

In our study, the incidence of side effects was more in Group LF as compared to Group LS. The incidence of side effects was zero in the magnesium group. Thus from Table 4, we concluded that magnesium provided a better side effect profile as compared to fentanyl and saline groups. Khezri et al.,[8] found the incidence of pruritus in two patients, hypotension in four patients, bradycardia in 0ne, and nausea in five patients belonging to Group F whereas none of the patients belonging to M group had any of these side effects. They concluded that magnesium provided a more stable hemodynamic profile and lesser side effects as compared to fentanyl. They attributed the absence of side effects to the slower onset of sympathetic blockade in the magnesium group. Raghu et al.,[16] and Unlugenc et al.,[17] also found that fentanyl had an increased incidence of side effects due to induction of central sensitization, such as hypotension, nausea, pruritus, or vomiting whereas none of the patients belonging to group magnesium experienced any of these effects. Hemalatha et al.,[11] compared different doses of magnesium sulfate (50 mg and 100 mg) for spinal anesthesia. The incidence of side effects such as hypotension and shivering was comparable between both the magnesium groups but were less as compared to the control group.

Limitations of the study

1. Pain being a subjective experience is impossible to be quantified with accuracy, thereby affecting its reliability as a statistical parameter. VAS scores, although an

attempt to quantify the descriptive nature of pain, still remain a subjective variable highly dependent on patients' self-reporting

2. All our study participants belonged to ASA Grade 1 or II and were aged between 18 and 60 years, and thus, our results may not be directly extrapolated to patients belonging to the extremes of age or ASA Grades III and IV.

CONCLUSION

The authors concluded that the addition of fentanyl and magnesium as adjuvants to intrathecal 0.5% hyperbaric levobupivacaine in patients undergoing lower limb surgeries significantly augmented the duration of analgesia as compared to levobupivacaine alone, but the addition of magnesium demonstrated fewer side effects as compared to both fentanyl and control groups.

ACKNOWLEDGMENT

We are thankful to our professors and all our colleagues for their valuable assistance and guidance throughout the period of our study. We are incredibly grateful to our patients, without whom this study would not have been possible.

REFERENCES

1. Bier A. Experiments in cocainization of the spinal cord. Dtsch Zschr Chir. 1899;51:363-369.
2. Whizar-Lugo VM, Íñiguez-López KL, Cárdenas-Maytorena AC and Ramírez-Puerta CD. Local anesthetics. In: Topics in Local Anesthetics. London: Intechopen; 2020. p. 1.
https://doi.org/10.5772/intechopen.80137
3. Morrison SG, Dominguez JJ, Frascarolo P and Reiz S. A comparison of the electrocardiographic cardiotoxic effects of racemic bupivacaine, levobupivacaine, and ropivacaine in anesthetized swine. Anesth Analg. 2000;90(6):1308-1314.
https://doi.org/10.1097/00000539-200006000-00009
4. Burm AG, Van der Meer AD, Van Kleef JW, Zeijlmans PW and Groen K. Pharmacokinetics of the enantiomers of bupivacaine following intravenous administration of the racemate. Br J Clin Pharmacol. 1994;38(2):125-129.
https://doi.org/10.1111/j.1365-2125.1994.tb04335.x
5. Tudorić Djeno I, Đuzel V, Ajduk M, Šafarić Oremuš Z, Župčić M, Dusper S, et al. Increase in specific density of levobupivacaine and fentanyl solution ensures lower incidence of inadequate block. Coll Antropol. 2012;36(2):375-380.
6. Vasure R, Ashahiya ID, Mahendra R, Narang N and Bansal RK. Comparison of effect of adding intrathecal magnesium sulfate to bupivacaine alone and bupivacaine-fentanyl combination during lower limb orthopedic surgery. Int J Sci Stud. 2016;3(10):141-146.
https://doi.org/10.17354/ijss/2016/28
7. Khandelwal M, Ahmed F and Sharma A. A comparative study of the effect of clonidine, fentanyl, and the combination of both as adjuvant to intrathecal bupivacaine for postoperative analgesia in total abdominal hysterectomy. J Anaesthesiol Clin Pharmacol. 2017;33(1):102-106.
https://doi.org/10.4103/0970-9185.202194
8. Khezri MB, Yaghobi S, Hajikhani M and Asefzadeh S. Comparison of postoperative analgesic effect of intrathecal magnesium and fentanyl added to bupivacaine in patients undergoing lower limb orthopedic surgery. Acta Anaesthesiol Taiwan. 2012;50(1):19-24.
https://doi.org/10.1016/j.aat.2012.03.001
9. Attri JP, Kaur G, Kaur S, Kaur R, Mohan B and Kashyap K. Comparison of levobupivacaine and levobupivacaine with fentanyl in infraumbilical surgeries under spinal anaesthesia. Anesth Essays Res. 2015;9(2):178-184.
https://doi.org/10.4103/0259-1162.152148
10. Goyal A, Shankaranarayan P and Ganapathi P. A randomized clinical study comparing spinal anesthesia with isobaric levobupivacaine with fentanyl and hyperbaric bupivacaine with fentanyl in elective cesarean sections. Anesth Essays Res. 2015;9(1):57-62.
https://doi.org/10.4103/0259-1162.150169
11. Hemalatha P, Banu N, Rao MH, Samantaray A, Venkatraman A and Hemanth N. Comparison of two different doses of magnesium sulphate for spinal anaesthesia: A prospective, randomized double-blind study. J Clin Sci Res. 2017;6(1):18-24.
https://doi.org/10.15380/2277-5706.JCSR.16.07.002
12. Khalili G, Janghorbani M, Sajedi P and Ahmadi G. Effects of adjunct intrathecal magnesium sulfate to bupivacaine for spinal anesthesia: A randomized, double-blind trial in patients undergoing lower extremity surgery. J Anesth. 2011;25(6):892-897.
https://doi.org/10.1007/s00540-011-1227-z
13. Gupta A, Tandon N, Jain N and Jindal M. Effect of addition of intrathecal preservative free magnesium sulfate with 0.5% bupivacaine heavy and fentanyl with 0.5% bupivacaine heavy on post-operative pain relief in patients undergoing hysterectomy. Asian J Med Sci. 2023;14(3):54-59.
https://doi.org/10.3126/ajms.v14i3.49054
14. Özalevli M, Cetin TO, Unlugenc HA, Guler T and Isik G. The effect of adding intrathecal magnesium sulphate to bupivacaine-fentanyl spinal anaesthesia. Acta Anaesthesiol Scand. 2005;49(10):1514-1519.
https://doi.org/10.1111/j.1399-6576.2005.00793.x
15. Katiyar S, Dwivedi C, Tipu S and Jain RK. Comparison of different doses of magnesium sulphate and fentanyl as adjuvants to bupivacaine for infraumbilical surgeries under subarachnoid block. Indian J Anaesth. 2015;59(8):471-475.
https://doi.org/10.4103/0019-5049.162982
16. Raghu R, Indira P and Vanaja. A Comparisoin of fentanyl citrate and magnesium sulphate as adjuvants to 0.5% heavy bupivacaine in spinal anaesthesia. Indian J Anesth Analg. 2019;6(1):323-332.
https://doi.org/10.21088/ijaa.2349.8471.6119.45
17. Unlugenc H, Ozalevli M, Gunduz M, Gunasti S, Urunsak IF, Guler T, et al. Comparison of intrathecal magnesium, fentanyl, or placebo combined with bupivacaine 0.5% for parturients undergoing elective cesarean delivery. Acta Anaesthesiol Scand. 2009;53(3):346-353.
https://doi.org/10.1111/j.1399-6576.2008.01864.x
18. Jain S. Double blinded clinical comparative trial of intrathecal dexmedetomidine and fentanyl as an adjuvant to isobaric levobupivacaine. Int J Med Anesthesiol. 2018;1(1):36-40.
https://doi.org/10.33545/26643766.2018.v1.i1a.213

Authors' Contributions:
AT- Literature survey, prepared the first draft of the manuscript, implementation of the study protocol, data collection, data analysis, manuscript preparation and submission of article; **NT**- Concept, design, clinical protocol, manuscript preparation, editing, manuscript revision and supervision; **NJ**- Design of study, statistical analysis and interpretation, revision of the manuscript; **DS**- Data collection, data analysis, manuscript revision, submission of article.

Work attributed to:
Gajra Raja Medical College, Gwalior, Madhya Pradesh, India.

Orcid ID:
Anusha Tripathy - https://orcid.org/0009-0009-3858-3778
Neelima Tandon - https://orcid.org/0000-0002-5544-2266
Namrata Jain - https://orcid.org/0000-0002-2212-4296
Devendra Singh - https://orcid.org/0009-0000-2322-9500

Source of Support: Nil, **Conflicts of Interest:** None declared.