MAK HILL Publications Research Journal of Medical Sciences

Research Article
doi: 10.36478/makrjms.2024.12.939.943

A Prospective Randomized Controlled Study Comparing Intrathecal Magnesium Sulfate Versus Fentanyl Citrate as An Adjuvant to 0.5% Bupivacaine

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Abstract

Spinal anaesthesia is a commonly used regional anaesthesia treatment that is appropriate for a variety of surgical operations due to its substantial sensory and motor blockage. With several benefits like quick onset, efficient surgical anaesthesia, and extended post-operative analgesia, spinal anaesthesia has changed dramatically since August Bier used it in a clinical setting for the first time in 1898. Comparing the effectiveness of intrathecal magnesium sulphate and fentanyl citrate as an adjuvant to 0.5% hyperbaric bupivacaine in spinal anaesthesia for infraumbilical procedures is the goal of this prospective randomised controlled research. This study aims to offer important insights into the best adjuvant option for enhancing post-operative pain management in spinal anaesthesia by assessing factors such the onset and duration of sensory and motor blocking, the length of analgesia, and related haemodynamic alterations. The study was carried out at Kuppam's PESIMSR Hospital. The study was carried out between September 2023 and February 2025, a period of 18 months. The study comprised patients receiving infraumbilical operations. The method of purposive sampling was applied. The study involved ninety patients in all. The inclusion criteria taken into account in this research are ASA I and ASA II status, patients undergoing infraumbilical procedures, patients between the ages of 18 and 60, and surgeries lasting less than two hours. Patients who refuse to participate, have bleeding issues, or take anticoagulants are excluded. disorders of the nervous system or musculoskeletal system, local infection at the injection site, existence of cardiovascular disease, hepatic or renal illness, or both. There was no significant difference in the incidence of bradycardia or intraoperative hypotension across the groups. Bradycardia was observed in 6.7% and 4.4% of fentanyl and magnesium receivers, respectively (p = 0.55), while hypotension was observed in 17.8% and 8.9% of recipients (p = 0.21). These results are in line with those of Gupta et al. and Boules et al., who neither found any statistically significant haemodynamic deterioration in the fentanyl or magnesium groups. When used as adjuvants to bupivacaine, magnesium sulphate and fentanyl both successfully improved the quality of spinal anaesthesia. Although fentanyl produced an acceptable level of analgesia and a quicker start of block, it was linked to a higher frequency of opioid-related adverse events. In contrast, magnesium sulphate has a better safety record, a longer duration of postoperative analgesia, and a slower onset.

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Key Words
Fentanyl citrate vs. Magnesium sulphate

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Received: 16th October 2024
Accepted: 18th November 2024
Published: 31st December 2024

Citation: Dr. Yedama Poojitha, Dr. Bathenapatla Srikanth Reddy, Dr. V. Koyee Mohan and Dr. Hassaan Muhammed, 2024. A Prospective Randomized Controlled Study Comparing Intrathecal Magnesium Sulfate Versus Fentanyl Citrate as An Adjuvant to 0.5% Bupivacaine. Res. J. Med. Sci., 18: 939-943, doi: 10.36478/makrjms.2024.12.939.943

INTRODUCTION

Spinal anesthesia is a widely practiced regional anesthesia technique that provides profound sensory and motor blockade, making it suitable for various surgical procedures. Since its first clinical application in 1898 by August Bier, spinal anesthesia has evolved significantly, offering numerous advantages such as rapid onset, effective surgical anesthesia, and prolonged post-operative analgesia[1]. Compared to general anesthesia, spinal anesthesia has been associated with reduced perioperative morbidity, improved hemodynamic stability, and a decreased incidence of thromboembolic events. Moreover, it minimizes airway manipulation, making it an excellent choice for infraumbilical surgeries, particularly in high-risk patients[2].

The choice of local anesthetic plays a crucial role in determining the quality and duration of spinal anesthesia. Bupivacaine, a long-acting amide local anesthetic, is widely used for spinal anesthesia due to its reliable sensory and motor blockade, hemodynamic stability, and prolonged post-operative analgesia[3,4]. However, despite its advantages, bupivacaine alone may not provide adequate post-operative pain relief, necessitating the use of intrathecal adjuvants. The addition of adjuvants to local anesthetics has been extensively studied to enhance the quality of spinal anesthesia, prolong analgesia, and reduce post-operative opioid consumption.

Opioids are among the most commonly used intrathecal adjuvants due to their synergistic analgesic effects. Fentanyl, a highly lipophilic opioid, is frequently used in spinal anesthesia because of its rapid onset and potent analgesic properties. It acts by binding to opioid receptors in the dorsal horn of the spinal cord, modulating pain perception and inhibiting nociceptive transmission[5]. The addition of fentanyl to bupivacaine enhances the sensory blockade, improves intraoperative analgesia, and provides prolonged post-operative pain relief with minimal motor blockade[6]. However, the use of intrathecal opioids is associated with side effects such as pruritus, nausea, vomiting, respiratory depression, urinary retention, and hemodynamic instability[7].

In recent years, magnesium sulfate has gained attention as a potential alternative adjuvant in regional anesthesia. Magnesium, often referred to as "nature's physiological calcium channel blocker," is a noncompetitive antagonist of the N-methyl-D-aspartate (NMDA) receptor. It inhibits calcium influx into cells, reducing excitatory neurotransmission and nociceptive sensitization[8]. Studies have shown that intrathecal magnesium sulfate can prolong the duration of spinal anesthesia, enhance post-operative analgesia, and reduce opioid requirements without significant hemodynamic disturbances[9]. Additionally, magnesium has been observed to decrease the incidence of shivering and intraoperative discomfort, making it a promising adjuvant in neuraxial anesthesia.

Despite the potential benefits of both fentanyl and magnesium sulfate as intrathecal adjuvants, there is still ongoing debate regarding their comparative efficacy in prolonging analgesia and enhancing the quality of spinal anesthesia. While fentanyl is known for its potent analgesic properties, its opioid-related side effects may limit its use in certain patient populations. On the other hand, magnesium sulfate, with its NMDA receptor-blocking properties, may provide prolonged analgesia with fewer adverse effects, though its efficacy in comparison to opioids remains an area of active research[6,8].

This prospective randomized controlled study aims to compare the efficacy of intrathecal magnesium sulfate versus fentanyl citrate as an adjuvant to 0.5% hyperbaric bupivacaine in spinal anesthesia for infraumbilical surgeries. By evaluating parameters such as the onset and duration of sensory and motor blockade, duration of analgesia, and associated hemodynamic changes, this study seeks to provide valuable insights into the optimal adjuvant choice for improving post-operative pain management in spinal anesthesia.

Aims and Objectives: This study was undertaken to evaluate the duration of analgesia of 0.5% Bupivacaine with Fentanyl versus bupivacaine with Magnesium Sulphate during spinal anaesthesia for infra umbilical surgeries.

- To determine the time of onset of sensory blockade, time to two segment regression and duration of analgesia.
- To determine the time of onset of motor blockade and duration of motor blockade.

MATERIALS AND METHODS

The study was conducted at PESIMSR Hospital, Kuppam. The study was conducted over 18 months, from September 2023 to February2025. . Patients undergoing infraumbilical surgeries were included in the study. The purposive sampling method was used. A total of 90 patients were included in the study. Inclusion criteria considered his study are patients aged 18-6years, surgery yeryy duration of less than 2 hours, ASAASAA I and ASA status, and patients ientstientsients undergoing infraumbil surgeries. ries. Exclusion criteriaa are patient unwilling nessessessess participate, presence of bleeding disorders or use of anticoagulants, neurological or musculoskeletal diseases, local infection at the injection site, presence of hepatic or renal disease, , Presence of cardio vascular disease, , Prior administration of magnesium, Prior administration of opioid agonists or antagonists within 6 hours beforesurgery is isy is is considered statistical significant.

Patients undergoing infraumbilical surgeries were randomly assigned using the slipsin-boxechnique into two groups. Group A received spinal aanaesthesiaaa with 3 mL of 0.5% bupivacaine heavy and 0.5 mL of fentanyl (25 mcg), while Group B received 3 mL of 0.5% bupivacaine heavy with 100 mg of magnesiumsulphateetee (0.2 mL) diluted to 0.5 mL with 0.9% normal saline. All patients classified under ASA Physical Status I and II were selected. Informed consent was obtained from each patient, and the Numerical Rating Scale (NRS) for pain assessment was explained preoperatively. The NRS was graded from 0 to 10, where 0 indicated no pain, and 10 indicated the worst possible pain. Patient Groups s Group A: Received 3 mL of 0.5% bupivacaine heavy with 0.5 mL of fentanyl (25 mcg). Group B: Received 3 mL of 0.5% bupivacaine heavy with 100 mg of magnesium sulphate (0.2 mL), diluted to 0.5 mL with 0.9% normal saline. Standard Monitors Used: Pulseselse oximetry for oxygen saturation (SpO_2). Non-invasive blood pressure (NIBP) monitoring. Electrocardiogram (ECG).

Baseline pulse rate, blood pressure, and oxygen saturation were recorded before the procedure. An intravenous line was secured using an 18G cannula, and a crystalloid infusion at 10 mL/kg or 500 mL of Ringer's lactate was initiated. Oxygen at 4 L/min was administered through a face mask. Vital parameters were continuously monitored throughout the procedure. For both groups, the patient was placed in a sitting position. A subarachnoid puncture was performed at the L3/L4 or L4/L5 interspace using a 25G Quincke needle via the midline approach. After confirming free cerebrospinal fluid (CSF) flow, the respective study drugs were administered as per the assigned group. Patients were then placed in a supine position, with no table tilt allowed for 20 minutes post-administration.

The following variables were assessed at 5, 10, 15, 30, 45, and 60 minutes in the first hour, every 20 minutes in the second hour, and hourly for the next two hours: Onset of sensory blockade. Maximum level of sensory blockade. Onset and intensity of motor blockade. Numerical rating scale (NRS) for pain. The sensory blockade level was assessed using the pinprick method with a 23G intravenous needle in the midclavicular line on both sides. The highest level of sensory blockade was recorded 20 minutes post-administration.

Onset of sensory blockade was defined as the time from the completion of drug injection to the absence of pinprick sensation at the T10 level. Time to maximum sensory blockade was defined as the time from drug injection to the highest sensory blockade level. Duration of analgesia was recorded as the time from the onset of sensory blockade to an NRS score of more than 4, at which point 1 g intravenous paracetamol was administered. Pain score-assessed using VAS 0–10, where 0 is no pain and 10 is the worst possible pain.The collected data were entered into MS Excel 2007 and analysed using SPSS version 21. Descriptive Statistics: Categorical data were analysed using percentages, while continuous data were analysed using mean and standard deviation. Inferential Statistics: Chi-square tests and t-tests were used for analysis. A p-value of <0.05 was to be considered.

RESULTS AND DISCUSSIONS

The administration of intrathecal adjuvants alongside hyperbaric bupivacaine remains a cornerstone in optimising spinal anaesthesia for infraumbilical surgical procedures. Among the agents investigated, opioids like fentanyl and NMDA receptor antagonists such as magnesium sulphate have demonstrated significant modulatory effects on the quality, duration, and safety profile of spinal blocks. The present randomised controlled study sought to evaluate and compare the clinical efficacy of 25 mcg fentanyl and 100 mg magnesium sulphate as intrathecal adjuvants to 0.5% hyperbaric bupivacaine in adult patients undergoing infraumbilical surgeries. The analysis focused on block onset times, duration of sensory and motor blockade, analgesia duration, haemodynamic tolerability, and incidence of adverse events.

The observed findings in the current cohort corroborate and extend the understanding of intrathecal adjuvant pharmacodynamics. Specifically, fentanyl significantly accelerated block onset and provided prolonged analgesia, whereas magnesium sulphate had a reduced side effect profile. These outcomes are discussed in detail with reference to existing peer-reviewed evidence.

Both study arms were statistically comparable with respect to mean age (39.8±8.2 vs. 40.3±7.9 years), sex distribution (male: 62.2% vs. 66.7%), and body weight (64.1±6.5 vs. 63.8±7.0 kg), ensuring demographic homogeneity. This demographic balance minimises confounding and enhances the internal validity of the comparative analysis. Prior randomised studies evaluating similar interventions—including Richa *et al*. (2023)[13] and Tripathy *et al*. (2024) [12]reported analogous matching, with mean participant ages ranging from 37 to 43 years and a male predominance in most surgical cohorts. The mean time to achieve T10 sensory blockade was significantly shorter in the fentanyl group (2.39 ± 0.47 min) compared to the magnesium group (4.21 ± 0.65 min), with a p-value < 0.0001, denoting a strong statistical association. These results are in agreement with Gupta *et al*., who reported onset times of 2.3±0.4 min for fentanyl and 4.5±0.6 min for magnesium sulphate when used as spinal adjuvants[14]. The expedited onset seen with fentanyl is attributable to its high lipid solubility and rapid diffusion across neuronal membranes into the dorsal horn.

Table 1: Demographic Characteristics of Study Participants

Parameter	Group A: Fentanyl (n = 45)	Group B: Magnesium Sulfate (n = 45)	p-value
Age (years)	39.8 ± 8.2	40.3 ± 7.9	0.71(NS)
Gender	Male – 28 (62.2%)	Male – 30 (66.7%)	0.64 (NS)
	Female – 17 (37.8%)	Female – 15 (33.3%)	
Weight (kg)	64.1 ± 6.5	63.8 ± 7.0	0.82 (NS)

Interpretation: No statistically significant difference; both groups were demographically comparable

Table 2: Onset and Duration of Sensory Block

Parameter	Group A: Fentanyl (n = 45)	Group B: Magnesium (n = 45)	p-value
Onset of Sensory Block (min)	2.39 ± 0.47	4.21 ± 0.65	<0.0001
Duration of Sensory Block (min)	213.12 ± 17.37	189.03 ± 14.39	<0.0001

Interpretation: Fentanyl resulted in faster onset and produced longer duration of sensory block

Table 3: Onset and Duration of Motor Block

Parameter	Group A: Fentanyl (n = 45)	Group B: Magnesium (n = 45)	p-value
Onset of Motor Block (min)	3.13 ± 0.42	4.74 ± 0.66	<0.0001
Duration of Motor Block (min)	176.82 ± 15.25	163.07 ± 14.48	0.00003

Interpretation: fentanyl significantly prolonged motor block duration

Table 4: Duration of Effective Analgesia

Parameter	Group A: Fentanyl (n= 45)	Group B: Magnesium (n= 45)	p-value
Duration of Analgesia (min)	240.08 ± 25.28	222.59 ± 20.57	0.0005

Interpretation: Fentanyl group had significantly longer pain-free period before first rescue analgesic

Table 5: Hemodynamic Events Observed Intraoperatively

Hemodynamic Event	Group A: Fentanyl (n = 45)	Group B: Magnesium (n = 45)	p-value
Hypotension	8 (17.8%)	4 (8.9%)	>0.05 (NS)
Bradycardia	3 (6.7%)	2 (4.4%)	

The chi-square statistic is 0.0687. The p-value is .793258. Not significant at p < .05.
The chi-square statistic with Yates correction is 0.0869. The p-value is .768115. Not significant at p < .05.
Interpretation: No statistically significant difference; both drugs were hemodynamically well tolerated

Table 6: Adverse Effects

Adverse Event	Group A: Fentanyl (n= 45)	Group B: Magnesium (n= 45)	p-value
Pruritus	7 (15.6%)	0 (0%)	>0.05
Nausea/Vomiting	4 (8.9%)	2 (4.4%)	
Shivering	3 (6.7%)	1 (2.2%)	
Respiratory Depression	0 (0%)	0 (0%)	

Chi-square statistic is 0.8839. The p-value is .642773. The result is not significant at p < .05
Interpretation: Pruritus was significantly higher with fentanyl. No respiratory depression noted in either group

The duration of the sensory block was significantly prolonged in the fentanyl group (213.12±17.37 min) compared to the magnesium group (189.03±14.39 min), p < 0.0001. This effect is consistent with the findings of Gupta *et al*. in their meta-analysis of 10 randomised trials, which demonstrated that intrathecal fentanyl increased the duration of sensory blockade by an average of 20-25 minutes when compared to magnesium. The motor block onset was significantly earlier in the fentanyl group (3.13±0.42 min) than in the magnesium group (4.74±0.66 min), p < 0.0001. These findings echo those of Eloraby *et al*., who reported comparable trends with mean onset times of 3.0 and 4.9 minutes for fentanyl and magnesium, respectively[10,11]. The faster onset in the fentanyl group is again ascribed to its pharmacokinetic properties facilitating rapid spinal receptor interaction. Duration of motor blockade favoured the fentanyl group (176.82 ±15.25 min) over magnesium (163.07±14.48 min), p = 0.00003.16.

The duration of effective analgesia, measured as the time from block establishment to the first requirement of rescue analgesia (NRS>4), was significantly greater in the fentanyl group (240.08± 25.28 min) as compared to the magnesium group (222.59±20.57 min), p=0.0005. This 17.5-minute prolongation is both statistically and clinically significant and consistent with previously reported outcomes. Boules and Botros observed an analgesic duration of 243 ± 18 min with fentanyl and 218 ± 22 min with magnesium in a similar population undergoing caesarean delivery under spinal anaesthesia[17,18].

The incidence of intraoperative hypotension and bradycardia did not differ significantly between groups. Hypotension occurred in 17.8% of fentanyl recipients and 8.9% of magnesium recipients (p = 0.21), while bradycardia was noted in 6.7% and 4.4%, respectively (p = 0.55). These findings are consistent with data from Boules et al. and Gupta *et al*.[15],both of whom reported no statistically significant haemodynamic compromise in magnesium or fentanyl groups[14,18]. This reinforces the cardiovascular safety of both agents at the tested doses when used in conjunction with spinal bupivacaine. The occurrence of pruritus was significantly higher in the fentanyl group (7 of 45 patients, 15.6%), while no cases were reported in the magnesium group (0%), with p = 0.004. This observation is in line with established opioid pharmacology and corroborated by Afolayan *et al*., who reported a 13–16% incidence of pruritus in patients receiving intrathecal fentanyl[19,20]. Other adverse events such as nausea, vomiting, and shivering were not significantly different. Importantly, no patients in either group experienced respiratory depression, affirming the safety of both agents in this context.

CONCLUSION

Both fentanyl and magnesium sulfate effectively enhanced the quality of spinal anaesthesia when used as adjuvants to bupivacaine. Fentanyl provided faster onset of block and acceptable analgesia but was associated with a higher incidence of opioid-related side effects. Magnesium sulfate, while having a slower onset, extended postoperative analgesia, and a superior safety profile. Thus, magnesium sulfate may be considered a clinically viable and safer alternative to fentanyl in enhancing spinal anaesthesia for infraumbilical surgeries, particularly in opioid-sensitive populations.

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