ASIAN JOURNAL OF PHARMACEUTICAL AND CLINICAL RESEARCH



COMPARISON OF SUBARACHNOID MAGNESIUM SULFATE AND FENTANYL AS ADJUVANTS WITH 0.5% HEAVY BUPIVACAINE FOR POSTOPERATIVE ANALGESIA IN INFRA-UMBILICAL SURGERIES

GAGANDEEP KAUR[®], SYED ZEESHAN HUSAIN RIZVI*, RAJ KRISHNA SRIVASTAVA, ABHAY KUMAR RANA

Department of Anesthesiology, MIMS, Barabanki, Uttar Pradesh, India. *Corresponding author: Dr. Syed Zeeshan Husain Rizvi; Email: zeeshan.rzv@gmail.com

Received: 12 March 2023, Revised and Accepted: 16 May 2023

ABSTRACT

Objectives: The objective of the study was to compare the efficacy of adjuvant use of subarachnoid fentanyl with the adjuvant use of subarachnoid magnesium sulfate as adjuvants to bupivacaine in subarachnoid block for infraumbilical surgeries in terms of: (1) Block characteristics, namely, time taken for onset of block and time taken for regression of block, (2) Hemodynamic stability in intra- and post-operative phase.

Methods: A total of 70 ASA I/II patients scheduled for infra-umbilical surgery were enrolled in the study and were randomized either to Group F (0.5 mL Fentanyl+3 mL 0.5% Bupivacaine) (n=35) or to Group M (0.5 mL 20% Magnesium sulfate+3 mL 0.5% Bupivacaine). Time to achieve onset of block, duration of block. Data were analyzed using the Chi-square and Independent samples, t'-test.

Results: Age of patients ranged from 18 to 55 years. The two groups were matched onset of sensory and motor block was significantly earlier in Magnesium sulfate group as compared to fentanyl group. Regression of motor and sensory block was significantly earlier in group where magnesium sulfate was used as an additive in contrast to fentanyl. No other complication except nausea (8.6%) and bradycardia (8.6%) was reported in any of the patient.

Conclusion: Although magnesium sulfate appears to be a relatively safer alternative than fentanyl for adjuvant use with hyperbaric bupivacaine for post-operative pain management and to facilitate better block characteristics; however, it fails to achieve the analgesic effect even comparable to fentanyl. Further studies with inclusion of a control group and with changed drug-dose combinations are recommended to find out a better alternative.

Keywords: Magnesium sulfate, Fentanyl, Bupivacaine, Subarachnoid blocks, Analgesia.

© 2023 The Authors. Published by Innovare Academic Sciences Pvt Ltd. This is an open access article under the CC BY license (http://creativecommons.org/ licenses/by/4.0/) DOI: http://dx.doi.org/10.22159/ajpcr.2023v16i8.48838. Journal homepage: https://innovareacademics.in/journals/index.php/ajpcr

INTRODUCTION

Infra-umbilical surgeries, particularly lower abdomen and lower limb surgeries, are generally performed under spinal anesthesia. Although regional anesthesia offers a much safer hemodynamics as compared to general anesthesia, yet advancements to search more safer and sideeffect free combinations are call of the day [1,2].

Spinal anesthesia has the definitive advantage that profound nerve block can be produced in a large part of the body by the relatively simple injection of a small amount of local anesthetic. Yet, spinal anesthesia is often criticized for its inability to offer post-operative pain control as it utilizes only local anesthetics which generally have relatively short duration of action. Therefore, supplementation with the help of addition of an adjuvant anesthetic/analgesic is required.

Bupivacaine is one of the common local anesthetics that are used in regional anesthesia, neuraxial anesthesia, and local infiltration. Bupivacaine is a useful local anesthetic to achieve the objectives of rapid onset and faster recovery, however, it seems to be less effective when it comes to curb the post-operative pain necessitating the need to add some adjuvants that augment its effect on post-operative pain [3,4].

Opioids are considered the first choice to augment the effect of local anesthetics such as bupivacaine during the spinal block.

Among different alternatives, magnesium sulfate has emerged as a useful adjuvant that can help in tackling the problem of post-operative pain without exerting additional adverse effects [5,6], however, its efficacy in comparison with fentanyl remains to be established in view of only a few comparative studies comparing these two drugs for their adjuvant role with bupivacaine.

Hence, the present study was planned to compare the efficacy of blockade, duration of analgesia in bupivacaine with magnesium sulfate versus bupivacaine with fentanyl in subarachnoid block for infraumbilical surgeries.

METHODS

Study design

Prospective randomized study.

Study duration

18 months.

Study population

Patients scheduled for infra-umbilical surgeries under subarachnoid block at the department of Anaesthesiology, mayo institute of medical sciences, Barabanki.

Inclusion criteria

- Scheduled for infra-umbilical surgery
- Age 18–55 years
- No gender discrimination (both gender included)
- ASA Grade I and II
- Consent for inclusion.

Exclusion criteria

- Refusal for participation
- ASA grade III and above
- History of drug allergies
- Opioid addicts
- Anatomical/Spinal deformities/malformations.

Methodology

The present study is a prospective randomized study conducted over a period of 18 months, comprising 70 patients. Pre-anesthetic evaluation of all the patients was done. Informed consent for participation in the research project was taken after proper explanation of procedure in their own language.

A total of 70 ASA I/II patients scheduled for infra-umbilical surgery fulfilling the inclusion criteria and giving consent for enrolment in the study were randomly divided into two equal groups (35 each). Of these, 35 patients were administered 0.5 mL fentanyl as adjuvant to 3 mL 0.5% hyperbaric bupivacaine (Group F) and rest 35 patients were administered 0.5 mL 20% magnesium sulfate as adjuvant to 3 mL 0.5% hyperbaric bupivacaine (Group M).

Time taken to achieve motor and sensory block was noted, intraoperative hemodynamic parameters were monitored. Postoperatively, time taken for regression of motor and sensory blocks, time to first rescue analgesic, and VAS scores for pain were monitored up to 24 h post-operative intervals.

Data analysis

Data were analyzed using SPSS 21.0 software. Chi-square test, independent samples t-test, and Mann–Whitney U-tests were used to compare the data.

RESULTS

- Addition of 100 mg 20% magnesium sulfate to 0.5% hyperbaric bupivacaine intrathecally, showed the quicker onset as well as regression of sensory and motor blockade, when compared to addition of fentanyl
- Addition of fentanyl at a dose of 25 mcg prolongs the duration of analgesia in contrast to magnesium sulfate
- Both additives had comparable hemodynamics, demand for rescue analgesia was earlier in magnesium sulfate group
- Apart from nausea in fentanyl group no other complication was seen in either group.

Table 1 Sensory blockade onset was significantly earlier in Group M (4.14 ± 1.51 min) as compared to Group F (5.09 ± 2.02 min).Motor blockade onset was significantly earlier in Group M (6.09 ± 1.40 min) as compared to Group F (9.00 ± 1.63 min).

Table 2 Mean time of regression of Sensory block of Group M patients was significantly earlier $(137.37\pm11.01 \text{ minutes})$ as compared to that of Group F $(305.40\pm12.30 \text{ minutes})$. Regression of Motor block as significantly earlier in Group M as compared to Group F $(200.69\pm8.79 \text{ vs. } 268.97\pm8.83 \text{ minutes})$.

DISCUSSION

Infraumbilical surgeries, particularly lower abdomen and lower limb surgeries, are generally performed under spinal anesthesia.

The regional anesthesia is administered through the help of local anesthetics. The choice of an ideal local anesthetic depends on the onset, recovery, post-operative analgesic effect, and adverse effect profile.

Opioids are considered the first choice to augment the effect of local anesthetics such as bupivacaine during the spinal block. Adjuvant use

Table 1: Between Group Comparison of Onset of Sensory and Motor Block

SN	Type of Block	Group F (n=35)		Group M (n=35)		Student 't' test	
		Mean	SD	Mean	SD	'ť	ʻp'
1. 2.	Sensory Motor	5.09 9.00	2.02 1.63	4.14 6.09	1.51 1.40	2.208 8.030	0.031 <0.001

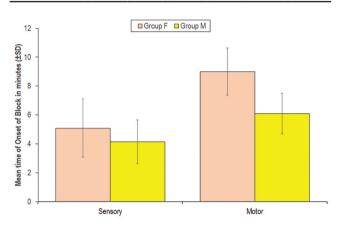
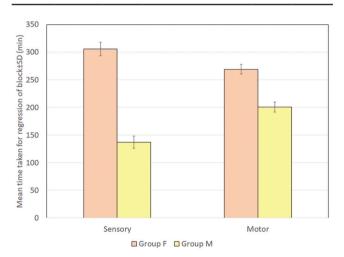


Table 2: Between Group Comparison of Regression of Sensory and Motor Block

SN	Type of Block	Group F (n=35)		Group M (n=35)		Student 't' test	
		Mean	SD	Mean	SD	'ť	ʻp'
1.	Sensory	305.40	12.30	137.37	11.01	60.777	< 0.001
2.	Motor	268.97	8.83	200.69	8.79	32.423	< 0.001



of fentanyl helps to reduce volatile agent requirements by more than twofold.

In the present study, the primary drug for spinal anesthesia was 3 mL of 0.5% hyperbaric bupivacaine. The two adjuvant drugs being compared were 0.5 mL fentanyl and 0.5 mL 20% magnesium sulfate, respectively.

Khezri *et al.* [8] too in their study used 3 mL 0.5% hyperbaric bupivacaine as the primary drug and 0.5 mL of $10\% \text{ MgSO}_4$ and 0.5 mL (25 µg) fentanyl as adjuvants. Yadav *et al.* [5] on the other hand though used 3 mL 0.5% bupivacaine as the primary drug; however, for adjuvant

they used 0.5 mL 25 μ g fentanyl but used two separate dosages of MgSO₄, 0.5 mL 10% MgSO₄ and 0.5 mL 20% MgSO₄, respectively. In other studies too, 0.5% hyperbaric bupivacaine has been used as the primary drug and 25 μ g fentanyl as the adjuvant, however, with respect to MgSO₄, there are slight differences. Katiyar *et al.* used 100 mg and 50 mg dosages of magnesium sulfate (20% and 10%), Aasim *et al.* and El-Moraaba *et al.* [11] used 10% magnesium sulfate while Rajola *et al.* [9] used 20% magnesium sulfate. Thus, most of the previous studies had experimented with the dose of magnesium sulfate while a standard dose of fentanyl was used. In the present study, we used 20% MgSO₄ to prove its efficacy and safety.

Block onset time

Both sensory and motor block onset times were significantly lower in magnesium sulffate as compared to fentanyl group of patients. This was similar to this study done by Yadav *et al.* [5] reported early block achievement in magnesium sulfate (20%) group but did not find a significant difference between fentanyl and 10% magnesium sulfate group.

Intraoperative hemodynamics and vital parameters

In the present study, we did not find a significant difference in hemodynamic and vital parameters between the two groups.

No adverse hemodynamic effect of magnesium sulfate use has been reported in earlier studies. Khezri et al. [8] in their study reported hemodynamic events such as hypotension and bradycardia in 1 (3.33%) and 4 (13.33%) patients, respectively, in the fentanyl group. In other study, Aasim et al. [10] and Rajola et al. [9] reported a better hemodynamic stability offered by magnesium sulfate as compared to fentanyl group. In the present study, no such marked superiority of one drug over the other was seen, probably owing to use of a relatively higher dose of magnesium sulfate. As such, the adjuvant use of intrathecal magnesium sulfate has not been reported to affect the hemodynamics and hence offers a better hemodynamic profile, the findings of the present study showed that magnesium sulfhate dosage up to 20% could be used safely without compromising the hemodynamics. El-Moraaba et al. [11] too in their study using various drug-dose combinations of fentanyl and magnesium sulfate did not find a significant difference in intra-operative hemodynamic profile of two groups.

Analgesic effect

In the present study, we found the rescue analgesic free time to be significantly longer in fentanyl as compared to magnesium sulfate group. Post-operative analgesic need was also significantly lower in fentanyl as compared to magnesium sulfate group. These findings showed that fentanyl provided a longer analgesic effect and fewer rescue analgesic needs as compared to magnesium sulfate.

In the present study, we found the duration of analgesic effect to be almost 1.25 times longer in fentanyl as compared to magnesium sulfate group. Compared to the present study, Khezri *et al.* [8] in their study reported to be 2.2 times longer in fentanyl as compared to magnesium sulfate group. However, they did not find a significant difference between the two groups with respect to post-operative analgesic use. The reason for this difference could be owing to two facts: first they used a lower concentration of magnesium sulfate (10%) as compared to that used in the present study (20%) that resulted in a relatively larger difference in duration of analgesia in their study as compared to that in the present study. Second, the post-operative follow-up period in their study was limited to 12 h only as compared to 24 h in the present study.

However, contrary to this stud and that of ours, Aasim *et al.* [10] found the adjuvant use of even 10% magnesium sulfate to be comparable to fentanyl in statistical terms but found duration to be longer in fentanyl group (1.2 times) as compared to that in the magnesium sulfate group. Moreover, in their study, there was no significant difference between the two groups with respect to rescue analgesic need. The reason for

the absence of statistically significant difference in duration of analgesia despite fentanyl group having a relatively longer duration as compared to fentanyl in their study could be owing to a smaller sample size. And also, their study included only lower abdominal surgeries as compared to all types of infraumbilical surgeries included in the present study.

The findings in the present study are in agreement with the observations made by Rajola *et al.* [9] who also used similar drug–dose combinations as used in the present study and found analgesic effects similar to ours.

In general, the findings of our study in the light of evidence from previous studies shows that even 20% magnesium sulfate use did not help to achieve similar analgesic effect as compared to fentanyl, though it maintained a similar hemodynamic profile.

Adverse effects

In the present study, nausea was noted in 3 patients in fentanyl group.

Khezri *et al.* [8] found magnesium sulfate group to be totally free of any adverse effect and noticed adverse effects only in fentanyl group. However, in their study, some serious side effects such as hypotension and bradycardia were noted in 13.3% and 3.3% of fentanyl group patients, nausea remained to be the most common adverse effect that was seen in fentanyl group in 16.7% of patients.

Some workers such as Yadav *et al.* [5] did not report of any side effect in any of their study groups. Detailed description of side effects of two groups has been reported by Rajola *et al.* [9] in their study who reported bradycardia as a side effect in 16% of magnesium sulfate as compared to none of the fentanyl group patients. However, other side effects such as hypotension, nausea, pruritus, and vomiting were seen in 28%, 4%, 6%, and 2% of fentanyl group patients as compared to none in the magnesium sulfate group patients.

CONCLUSION

The findings of the present study show that, although magnesium sulfate appears to be a relatively safer alternative than fentanyl for adjuvant use with hyperbaric bupivacaine for post-operative pain management and to facilitate better block characteristics; however, it fails to achieve the analgesic effect even comparable to fentanyl. Further studies with inclusion of a control group and with changed drug-dose combinations are recommended to find out a better alternative.

ETHICAL ISSUES

No ethical issues have been found to be occurring in this study.

CONFLICTS OF INTERESTS

No conflicts of interests have been found to be occurring.

FINANCIAL SUPPORT AND SPONSORSHIP

No financial support. Sponsorship has been obtained.

REFERENCES

- Elia N, Culebras X, Mazza C, Schiffer E, Tramèr MR. Clonidine as an adjuvant to intrathecal local anesthetics for surgery: Systematic review of randomized trials. Reg Anesth Pain Med 2008;33:159-67.
- Boussofara M, Carlès M, Raucoules-Aimé M, Sellam MR, Horn JL. Effects of intrathecal midazolam on postoperative analgesia when added to a bupivacaine-clonidine mixture. Reg Anesth Pain Med 2006;31:501-5.
- Morgan GE Jr., Mikhail MS, Murray MJ, Larson CP Jr. Clinical Anaesthesiology. 4th ed. USA: Lange Publisher; 2002.
- Chattopadhyay A, Maitra S, Sen S, Bhattacharjee S, Layek A, Pal S, *et al.* A study to compare the analgesic efficacy of intrathecal bupivacaine alone with intrathecal bupivacaine midazolam combination in patients undergoing elective infraumbilical surgery. Anesthesiol Res Pract 2013;2013:567134.

- Yadav M, Kumar PB, Singh M, Gopinath R. Intrathecal magnesium sulfate as a spinal adjuvant in two different doses, combined with 0.5% heavy bupivacaine for infraumbilical surgeries. Anesth Essays Res 2015;9:364-8.
- Banihashem N, Hasannasab B, Esmaeili A, Hasannasab B. Addition of intrathecal magnesium sulfate to bupivacaine for spinal anesthesia in cesarean section. Anesth Pain Med 2015;5:e22798.
- Harukuni I, Yamaguchi H, Sato S, Naito H. The comparison of epidural fentanyl, epidural lidocaine, and intravenous fentanyl in patients undergoing gastrectomy. Anesth Analg 1995;81:1169-74.
- Khezri MB, Yaghobi S, Hajikhani M, 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;50:19-24.
- 9. Yadav M, Kumar PB, Singh M, Gopinath R. Intrathecal magnesium

sulfate as a spinal adjuvant in two different doses, combined with 0.5% heavy bupivacaine for infraumbilical surgeries. Anesth Essays Res. 2015;9:364-8.

- Rajola R, Pacharla I, Vanaja. A Comparison of fentanyl citrate and magnesium sulphate as adjuvants to 0.5% heavy bupivacaine in spinal anaesthesia. Indian J Anesth Analg 2019;6:323-33.
- Aasim SA, Reddy S, Reddy M, Kumar KA, Vishnu, Rao S. A comparative study of the different doses of magnesium sulphate and fentanyl as adjuvants to bupivacaine [0.5% heavy] for lower abdominal surgeries under subarachnoid block. J Evol Med Dent Sci 2016;5:1735-8.
- El-Moraaba HA, Mamdouh AA, Sayed MA. Comparison between 3 different doses of magnesium sulphate as a spinal adjuvant to bupivacaine and fentanyl combination in lower limb orthopedic surgery. Med J Cairo Univ 2018;86:3253-62.