ORIGINAL RESEARCH

Comparison of premixed and sequential intrathecal buprenorphine with hyperbaric bupivacaine for abdominal hysterectomy surgeries

[1]Dr. Geetha S Hasaraddi, [2]Dr. Charulatha, [3]Dr. Pratibha SD, [4]Dr. Ragini K P, [5]Dr. Ramdas B

[1]Associate Professor, [2]Assistant Professor, [5]Professor, Department of Anaesthesiology and Critical Care, Navodaya Medical College, Raichur, Karnataka, India
[3]Associate Professor, Department of Anaesthesiology, BLDEDU's Shri BM Patil Medical College Hospital and Research Center, Vijayapur, Karnataka, India
[4]Senior Resident, Department of Anaesthesiology and Critical Care, Vijayanagar Institute of Medical Science, Bellary, Karnataka, India

Corresponding author
Dr. Pratibha SD
Associate Professor, Department of Anaesthesiology, BLDEDU's Shri BM Patil Medical College Hospital and Research Center, Vijayapur, Karnataka, India
Email: pratibhakaradi@gmail.com

Received: 19 June, 2023 Accepted: 21 July, 2023

ABSTRACT

Background: Relief of pain during surgery and in postoperative period is an aspect in surgical patients to make surgery uneventful. Few studies have observed that premixing adjuvants with local anaesthetic can alter the spread of the drug in the CSF. Hence administering adjuvants in separate syringes may reduce the change in density of both the drugs, which will prevent alteration in CSF spread. Hence the aim of this study is to evaluate the efficacy of intrathecal hyperbaric Bupivacaine with Buprenorphine premixed and sequentially to compare post-operative analgesia and rescue analgesia required over 24 hrs. **Methods:** This is a prospective, randomized single blind study involving 100 patients posted for elective total abdominal hysterectomy surgeries under spinal anaesthesia with ASA I and II, not known allergy to local anaesthetic, no infection at the site of injection. VAS score and vital parameters such as HR, NIBP, and $SP0_2$ were recorded in intra-operative and post-operative period. Blockade characteristics were recorded intra-operatively. **Results:** Mean heart rate, MAP, along with duration of time of onset of sensory block, motor block, Time for maximal blockade and regression time to T10 between two groups was compared and the difference was statistically significant. In the both groups VAS values were statistically significant at 4 hours, 6 hours, and 12 hours; however, group S had better postoperative pain relief than group M. **Conclusion:** We observed that sequential administration of buprenorphine with hyperbaric bupivacaine results in earlier onset of action, prolonged duration of sensory and motor blockade, prolonged duration of postoperative analgesia and less number of rescue analgesia when compared with administration of premixed buprenorphine with hyperbaric bupivacaine.

Keywords: Bupivacaine, Buprenorphine, Spinal Anaesthesia, Premixed and Sequential.

INTRODUCTION

Spinal anesthesia has well-defined end points and anaesthesiologists can produce the blocks with a single injection[1].It is commonly used in elective and emergency surgeries, because of its simplicity, rapidity, better pain control, early recovery of bowel function, fewer side effects, economical, and ease of administration.

Pain relief during surgery is the mainstay in anesthesia. Perioperative pain relief is the most important aspect for anaesthesiologists. Relief of pain during surgery and in the postoperative period is an aspect in surgical patients to make surgery uneventful. Bupivacaine is a commonly used drug in spinal anesthesia. Although other agents like ropivacaine, levobupivacaine also be used. Because of the short duration of action, these drugs are added with different adjuvants like Buprenorphine[2,3,4,] , Clonidine[5], ketamine[6], midazolam[2], Dexmedetomidine, Fentanyl, Mgso4[7,8] for

prolongation of intraoperative and postoperative analgesia[9]. However, each drug has its limitations and a need for alternative methods or drugs always exists.

It is common practice to add adjuvant drugs in the same syringe along with local anaesthetics. Mixing both adjuvant and local anaesthetic drugs in a single syringe might change the density of both the solution, hence will affect the spread of the drug in the cerebrospinal fluid (CSF). Administering adjuvant and local anaesthetic solutions in separate syringes will reduce the effect of change in density[2].

Opioids when administered as adjuvants with local anaesthetic solution intrathecally show synergistic action by increasing the sensory block without affecting sympathetic blockade. Buprenorphine is a mixed agonist-antagonist opioid with high affinity at both mu and kappa opiate receptors. Administering buprenorphine with local anaesthetic for spinal anaesthesia is very useful due to itshigh lipid solubility and affinity for opioid receptors. This leads to an increase in the duration of the action of analgesia and helps in managing postoperative pain.

Some adverse effects are observed due to the administration of buprenorphine which can be treated without much concern.

Some studies have observed that premixing adjuvants with a local anaesthetic solution may alter the spread of the drug in the CSF. Hence administering adjuvants in separate syringes may reduce the change in density of both drugs, which will prevent alteration in CSF spread[10].

Hence this study aims to evaluate the efficacy of intrathecal hyperbaric Bupivacaine with Buprenorphine premixed and sequentially administered in separate syringes to compare post-operative analgesia and rescue analgesia required over 24 hrs.

The primary objective of our study is Spinal block characteristics and Intraoperative hemodynamics. Secondary objectives are Postoperative analgesia, Rescue analgesia, and VAS score over 24hrs in patients posted for elective total abdominal hysterectomy surgeries by administering Buprenorphine and hyperbaric Bupivacaine as a premixed (Group M) and sequentially (Group S).

MATERIALS AND METHODS

This is a prospective, randomized single-blind study involving 100 patients posted for elective total abdominal hysterectomy surgeries under spinal anaesthesia carried out in our institution in the department of Anaesthesiology after obtaining institutional ethical clearance and written informed consent from all patients.

Inclusion criteria included, Patients posted for elective abdominal hysterectomy surgeries ASA (American Society of Anaesthesiology) Physical Status I and II patients, not a known allergic to local anaesthetic, no infection at the site of injection and Patients who have given consent.

Patient refusal, patients with coagulopathies, patients with vertebral column abnormalities, local sepsis, or significant neurological deficits and Patients with increased intracranial pressure were excluded from the study.

All the patients underwent pre-anaesthetic evaluation a day before surgery which included a detailed history taking and general physical examination. Systemic examination included respiratory, cardiovascular and central nervous systems. Spine was examined for deformity and infection at the procedural site. Investigations included Complete Blood Count, Blood Urea, Serum Creatinine and Electrocardiogram(ECG) and chest X- ray if required.

Patients were explained about the procedure and also how the visual analogue scale (VAS) aids in knowing postoperative pain.

Patients were kept nil by mouth overnight. and tab alprazolam 0.5mg was also given the night before surgery.

In preoperative room, all vital parameters were recorded such as heart rate, non-invasive blood pressure (NIBP), SpO_2, and ECG. An IV line was secured with a 20G cannula and patients were preloaded with Lactated Ringer's solution 10ml/kg.

In the operating room, all the monitors were connected which included Heart rate (HR), ECG, NIBP and SpO_2.

The anaesthetic technique was standardized for all patients. Spinal anaesthesia was administered in the left lateral position in the lumbar region at L3-L4/ L4-L5 intervertebral spaces in the median approach with a 23/25 Gauge spinal (Quincke) needle under strict aseptic precautions. The study drug was injected after the free flow of CSF. Patients were positioned supine after injection. Patients in group M received a mixture of 3ml of hyperbaric Bupivacaine premixed with 0.5ml (150µg) of Buprenorphine in a 5ml syringe. Patients in group S received 0.5ml (150µg) of injection Buprenorphine in a 2ml syringe followed by 3ml of hyperbaric Bupivacaine through a separate 5ml syringe. After spinal anaesthesia, intraoperatively all vitals were recorded. HR, oxygen saturation, and NIBP were recorded at 1min, 5 mins, 15 mins and 30 mins

The Pinprick method was used to assess the degree of sensory blockage until it reached the T6 level. The level was monitored every two minutes till it reached maximal sensory blockade.

The Bromage scale was used to evaluate the motor block. Score 0: The patient can move their hip, knee, and ankle. Score 1: The patient can move their knee and ankle but not their hip. Score 2: The patient can move their ankle but not their hip or knee. Score 3: The patient can't move their hip, knee, or ankle. Surgery started when the desired anaesthetic level was reached.

The period between the end of the anaesthetic injection and the loss of sensation to a pinprick at the T10 level was used to determine the beginning of

sensory blockage. The period between the end of the study drug injection till the attainment of bromage I was used to determine the onset of motor blockage.
The duration between the end of the study drug injection and the time when the block reached the T6 dermatome was used to define the maximal sensory blockade attainment.
The period between the end of the study drug injection and registration of Bromage grade 3 was used to define the maximum motor blockage reached.
Mephentermine 6 mg IV in incremental dose was givento treat hypotension, which is defined as a drop in systolic blood pressure of 20% or more from baseline. Injection atropine IV was given when the heart rate decreases by ≥ 20% of baseline.
After complete attainment of anaesthesia surgery was started. Both the sensory and motor levels were noted after the completion of the surgical procedure. Regression to level T10 and two-segment regression time from the maximum level were also recorded.
Duration of regression time to T10 was defined as the interval between the intrathecal injection to VAS >0 to<2 and the interval between VAS >1 to <4 for the duration of effective analgesia.
Score- 0-2 No pain, Scores of 2-4 indicate mild pain, 4-6 indicate moderate pain, 6-8 indicate severe pain and 8-10 indicate intolerable pain.
Following surgery, patients were routinely observed in the recovery and postoperative ward to assess their level of pain using the VAS scale over the course of 24 hours.
Duration of the first rescue analgesia was taken as the time from the intrathecal injection to VAS >4 and the number of rescue analgesia required over 24 hrs was taken when VAS score was more than 4 in both the groups.
VAS score and vital parameters such as HR, NIBP, and $SP0_2$ were recorded in the recovery room following surgery and then all vitals were noted at 4hrs,6hrs,12hrs, and 24hrs in the postoperative care unit.
When the VAS score > 4, a 100ml IV infusion of paracetamol was administered as rescue analgesia.
In both intraoperative and postoperative periods, side effects such as nausea, vomiting, pruritus, respiratory depression, urine retention, hypotension, and bradycardia were recorded.

STATISTICAL ANALYSIS:
Based on a study conducted by Archana S[3] showed that mean time taken to reach sensory block was 7.3±2.5 and 7.6±2.2 for premixed and sequential group respectively. According to the above findings with the power of 90% and α error of 5% of 100 ASA grade I/II/III patients who had been scheduled for elective abdominal hysterectomy were randomly allocated into two groups by computer generated random table with 50 patients in each group.
GROUP M - patient received a mixture of 3ml of hyperbaric Bupivacaine premixed with 150µg of Buprenorphine in a 5ml syringe.
GROUP S - patient received 150µg of injection Buprenorphine in a 2ml syringe followed by 3ml of hyperbaric Bupivacaine through a separate 5ml syringe.
Microsoft Excel was used to enter the data, and SPSS 22 version was used for data analysis.
Both the Student's t-test and the Chi-square test were used to assess the demographic data. The student's t-test was used to examine the quantitative data, and the Chi-square test was used to analyze the qualitative data. The mean and standard deviation were used to express all values. $P < 0.05$ was considered statistically significant.
Using the statistical formula:
$n=4pq/L^2$
where P = Prevalence / positive factor
q = Non prevalencei.e 1-P
L = Probable error, maximum upto 20%

RESULTS
In our study, a total of 100 patients, the mean age of the patients in Group M was 46.74±8.38 years and that of patients from Group S was 44.90±6.73 years. We compared the mean age between the two groups, the difference was statistically not significant (Table - 1).

Table 1: Demographic Data

	GROUP M(n=50)	GROUP S(n=50)	p-value
Age (Mean±SD)	46.74±8.38	44.90±6.73	0.229
ASA Grading -I	31(62%)	29 (58%)	-
ASA Grading -II	19(38%)	21(42%)	-
Height(cms)	157.54±4.14	158.60±4.21	0.207
Weight(kgs)	60.76±7.49	62.12±8.12	0.386
Duration of surgery (mins)	130.90±12.11	131.20±10.25	0.893

Data is represented as numbers and n(%),*p-value- <0.05 significant, Group M-Premixed Group S- Sequential.
Mean weight, height, ASA grading, duration of surgery were compared in the both groups and the difference was statistically not significant (Table-1).
Mean heart rate was compared at different time intervals in both the groups and found to be significant statistically at 5mins, 10mins, 15mins and 30mins (Figure-1).

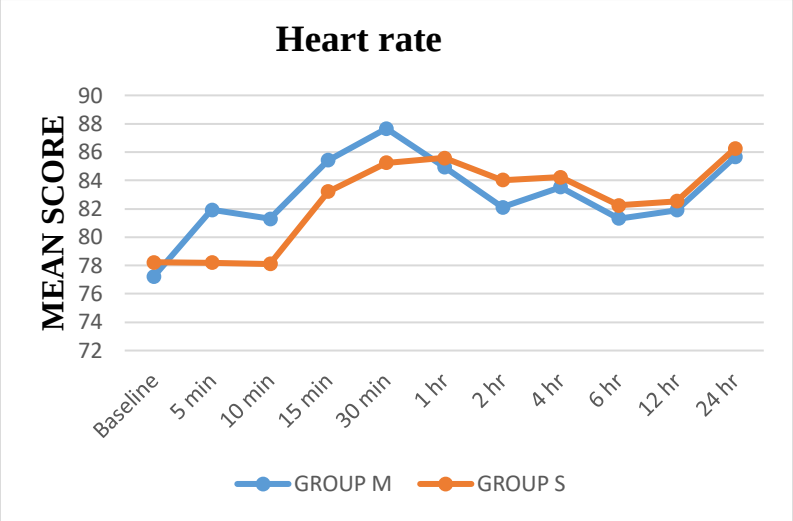

Figure 1: Line diagram of Mean Heart rate

Data is represented by line diagram. Group M- Premixed, Group S-Sequential .There was statistically significant difference in heart rate at 5mins, 10mins, 15mins and 30 mins.

Mean arterial pressure was compared in both groups at different time intervals was found to be statistically significant at 5mins,10mins, 15mins and 30mins (Table-2).

Table- 2: Mean arterial pressure

Time interval(in min)	Group M mean±S.D	Group S mean±S.D	P-Value
Baseline	95.1±2.21	94.2±2.01	0.035
5 min	88.03±3.14	91.6±2.88	<0.05
10 min	90.1±3.17	93.66±2.11	<0.05
15 min	91.1±2.13	93.46±2.21	<0.05
30 min	92.1±3.13	94.66±2.12	<0.05
60 min(1hr)	95.72±4.30	96.32±4.72	0.508
120 min(2hr)	98.56±7.59	98.10±1.25	0.673
240 min(4hr)	99.36±7.08	99.10±6.82	0.852
360 min(6hr)	97.36±4.09	97.64±4.29	0.739
720 min (12hr)	95.92±6.39	96.12±6.30	0.875
1440 min (24hr)	94.92±5.21	95.08±5.76	0.884

Data is represented as Mean±SD,*p-value- <0.05 significant, Group M-Premixed Group S-Sequential. There was statistically significant difference in MAP at 5mins, 10mins, 15mins and 30 mins.

The mean duration of time of onset of the sensory block between the two groups was compared the difference was statistically significant. Duration of onset of sensory block in Group S was significantly less as compared to Group M(Table -3).

Table 3: Time of sensory and motor block

	Group M mean±S.D (n=50)	Group S mean±S.D (n=50)	p-Value
Time of onset of sensory block (mins)	6.02±0.78	3.69±0.62	< 0.05*
Time of onset of motor block (mins)	7.55±0.86	5.73±0.61	< 0.05*
Time to reach maximal sensory block(mins)	8.99±0.91	6.90±0.61	< 0.05*
Regression time to T10 (mins)	137±2.7	160±3.4	<0.05*
First rescue analgesia (mins)	295.80±18.44	353.40±18.72	< 0.05*
Number of rescue analgesia	2.96±0.20	2.64±0.20	< 0.05*

Data is represented as Mean±SD,*p-value- <0.05 significant, Group M-Premixed GroupS-Sequential.

The mean duration of time to reach maximal sensory block between the two groups was compared there was a significantdifference statistically. The duration of time to reach the maximal sensory block in Group S was significantly less as comparedto Group M (Table-3).

The mean duration of time of onset of motor block was compared in both the groups the difference was statistically significant. Duration of onset of motor block in Group S was significantly less as compared to Group M(Table-3).

The mean duration of maximal motor block in both groups was comparedthe difference was statistically significant. Duration of onset of motor block in Group S was significantly less as compared to Group M (Table-3).

Mean regression time to T10 in both groups was compared there was a significant difference statistically. The duration of regression time to T10 in Group S was significantly higher as compared to Group M (Table-3).

We compared the mean duration of the first rescue analgesic required between the two groups, the difference was statistically significant. The duration of the first rescue analgesic required in Group S was significantly higher as compared to Group M (Table-3).

We compared the mean number of rescue analgesia between the two groups, the difference was statistically significant. The number of rescue analgesia in Group S was significantly less as compared to Group M(Table-3).

In the both groups VAS values were statistically significant at 4 hours, 6 hours, and 12 hours; however, group S had better postoperative pain relief (lower VAS) than group M(Figure-2).

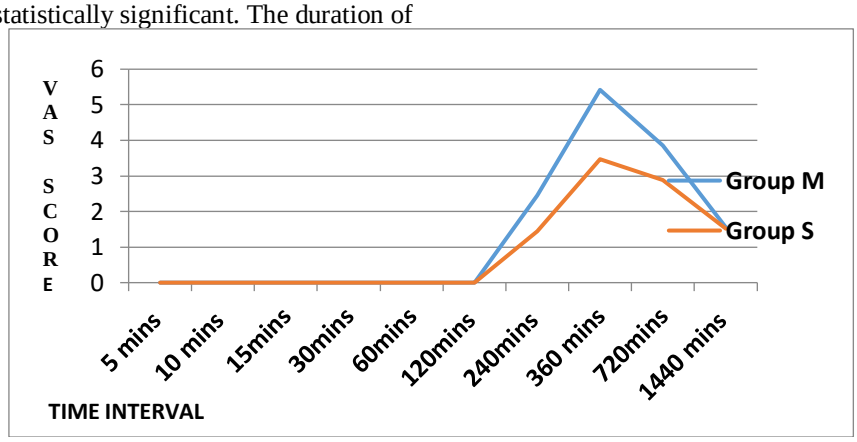

Figure 2: Line diagram of VAS Score

Data is represented by line diagram. Group M- Premixed , Group S-Sequential . There was statistically significant difference in VAS Score at 4hrs, 6hrs and 12 hrs.

Adverse effects were observed and hypotension prevalence was 72% in Group M as compared to 52% in Group S. Hypotension cases were seen more in Group M (Table-4).

Table 4: Adverse Effects

	Group M (n=50)	Group S (n=50)
Hypotension	36(72%)	26(52%)
Nausea/vomiting	8(16%)	15(30%)
Respiratory depression	0	0
Pruritus	0	0

Data is represented as numbers and n(%),*p-value-<0.05 significant, Group M-Premixed Group S-Sequential.

The prevalence of Nausea and Vomiting was 30% in Group S as compared to 16% in Group M. More number of Nausea and Vomiting cases were seen in Group S (Table-4).

This is because, in the premixed group the vomiting centers were inhibited by hyperbaric bupivacaine and hence buprenorphine did not stimulate the vomiting(CTZ) centers whereas in the sequential group, sincebuprenorphine is given before hyperbaric bupivacaine, it stimulated the vomiting(CTZ) centers and caused more incidence of nausea and vomiting.

Respiratory depression and pruritis were not seen in both groups (Table-4).

DISCUSSION

Our study was done to evaluate the efficacy of intrathecal hyperbaric Bupivacaine with Buprenorphine premixed and sequentially administered in separate syringes to compare post-operative analgesia and rescue analgesia required over 24 hrs.

When treating moderate to severe post-operative pain, buprenorphine works well as an adjuvant to intrathecal local anesthetic.

Buprenorphine is good as an adjuvant to intrathecal local anesthetic for managing moderate to severe postoperative analgesia.

According to studies, adding adjuvants to hyperbaric bupivacaine may change its spreads in the CSF. On the other hand, sequential administration of adjuvants in separate syringes may limit the change in density of both drugs, preventing any change in CSF spread[10].

When compared to the administration of premixed buprenorphine with hyperbaric bupivacaine, Archana Shivashankar et al[3] found that sequential administration of buprenorphine with hyperbaric bupivacaine results in earlier onset of action, prolonged duration of sensory blockade, and extended duration of postoperative analgesia.

Borse Y M et al [11]conducted a study to compare intrathecal bupivacaine alone and Bupivacaine premixed with buprenorphine(150µg) for

postoperative analgesia in orthopedic surgeries and found that buprenorphine added to Bupivacaine hyperbaric have effective and considerably prolonged postoperative analgesia.

With reference to the above studies, the following study was conducted, since no similar studies were available with the patients undergoing Total Abdominal Hysterectomy.

In our study, the mean arterial pressure decreased in both groups but was much lower in the sequential group than in the mixed group and Group M also required more vasopressors. This could be explained by the fact that the sequential group had a higher block level, which led togreatersympathetic blockade hence a greater fall in blood pressure.

In our study patients who received Bupivacaine premixed with buprenorphine had considerably higher pain scores earlier than patients who received Bupivacaine with sequential buprenorphine combinations as assessed by VAS.

In a study by Cesuretet al [12] on the effects of sequential administration ofhyperbaric and plainbupivacaine in parturients, it was foundthat patients who received the drugs sequentially hadexperienced less hypotension andvasopressor requirement was less.

Arora MV et al [13]compared the duration of analgesia, sensory block, and motor block in lower limb surgeries after intrathecal administration of clonidine-bupivacaine (Group C), buprenorphine-bupivacaine (Group B), and bupivacaine alone (Group A), and discovered that buprenorphine has a long-lasting effect.

The effectiveness of premixed versus sequential administration of dexmedetomidine as an adjuvant to intrathecal hyperbaric bupivacaine was done in a similar study by Gunjan Chaudhry et al [10] ,they found that the time to achieve T10 spinal level was significantly shorter in the sequential group than in the premixed group. Similarly, patients in the sequential group achieved Modified Bromage III earlier than group P.

A study by SoumyaSamalet al [14] showed that when intrathecal buprenorphine and intrathecal dexmedetomidine were compared for postoperative analgesia in lower abdominal and lower limb surgeries. Group B received intrathecal 150 g Buprenorphine along with 15 mg of heavy 0.5% Bupivacaine, while Group D received intrathecal 15 g dexmedetomidine along with 15 mg of heavy 0.5% bupivacaine and observedthat period for first rescue analgesia in the postoperative period was much longer in group B than group D[15].

With all the above observations, we observed that sequential administration of 150mcg buprenorphine with 0.5% hyperbaric bupivacaine results in early onset of action, prolonged duration of sensory and motor blockade, and increasedduration of postoperative analgesia when compared with administration of premixed 150 mcg buprenorphine with 0.5% hyperbaric bupivacaine.

Our study's limitation is that we could not measure the drug density and temperature before injecting them, both of which could alter the spread of the drug in the CSF.

The effects of administering buprenorphine before bupivacaine on the block characteristics were not observed.

CONCLUSION

In our study, we observed that sequential administration of buprenorphine with hyperbaric bupivacaine results in earlier onset of action, prolonged duration of sensory and motor blockade, prolonged duration of postoperative analgesia, and less number of rescue analgesia when compared with administration of premixed buprenorphine with hyperbaric bupivacaine.

REFERENCES

1. Brown DL, Spinal block in Atlas of Regional Anaesthesia, 2nd Edition, Philadelphia, WB Saunders Company,1999.
2. Dhakshinamoorthy, V Anandaraj. A comparative study between the efficacy of fentanyl with bupivacaine 0.5%, buprenorphine with bupivacaine 0.5%, and midazolam with bupivacaine 0.5% in spinal anesthesia for lower abdominal surgeries.MedPulse International Journal of Anesthesiology. October 2018; 8(1): 06-11
3. Archana Shivashankar1, PraptiRath2 ,Sadashivan S. Iyer3 , CVR Mo han. Combination of buprenorphine with hyperbaric bupivacaine administered either as a mixture or sequentially for spinal anaesthesia for caesarean section. Indian Journal of Clinical Anaesthesia, 2017;4(3): 291-297
4. Ravindran R, Sajid B, Ramadas KT, SusheelaI. Intrathecal hyperbaric bupivacaine with varying doses of buprenorphine for postoperative analgesia after cesarean section: A comparative study. Anesth Essays Res 2017;11:952-7.
5. Prashant Lomate, Jyotsna Paranjpe, Shilpa Gaikwad. Comparison of the efficacy of intrathecal buprenorphine and clonidine as adjuvants to bupivacaine for postoperative analgesia and abdominal muscle relaxation in patients of abdominal hysterectomy. Med Pulse International Journal of Anesthesiology. March 2019; 9(3): 201-207.
6. SunandaPanigrahi, ArchanaMhatre. Comparative study between ketamine and bupivacaine intrathecally in the lower abdomen and lower limb surgery. IAIM, 2018; 5(8): 47-54
7. Gupta R, Verma R, Bogra J, Kohli M, Raman R, Kushwaha JK. A Comparative study of intrathecaldexmedetomidine and fentanyl as adjuvants to Bupivacaine. J AnaesthesiolClinPharmacol. 2011;27(3):339–343. doi:10.4103/0970-9185.83678
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(3):e22798. Published 2015 Jun 22. doi:10.5812/aapm.5(3)2015.22798.
9. Richard Brull, Alan J.R. Macfarlane, and Vincent W.S. Chan. Spinal, Epidural, and Caudal Anesthesia.

Chapter 45 In Miller's Anaesthesia, 9th edn.,vol1, edt., Miller RD. Philadelphia;Elsevier,2020:p.1413-1449

10. Chaudhry, Gunjan &Singla, Deepak &Dureja, Jagdish& Bansal, Pranav & Ahuja, Kirti. (2016). Efficacy of premixed versus sequential administration of dexmedetomidine as an adjuvant to intrathecal hyperbaric bupivacaine in lower limb surgery. Southern African Journal of Anaesthesia and Analgesia. 22. 1-5. 10.1080/22201181.2016.1179468
11. Borse, Y., Thorat, S.A., Dighe, J., &Patil, P. (2015). A comparative study of intrathecal Bupivacaine and Bupivacaine with Buprenorphine for postoperativeanalgesia in orthopedic surgeries. Indian Journal of Clinical Anaesthesia, *2*, 92-96.
12. Cesur M, Alici HA, Erdem AF, Borekci B, Silbir F. Spinal anesthesia with sequential administration of plain and hyperbaric bupivacaine provides satisfactory analgesia with hemodynamic stability in caesarean section. Int J ObstetAnesth 2008;17:217-22.
13. Arora MV, Khan MZ, Choubey MS, Rasheed MA, Sar kar A. Comparison of spinal block after intrathecal clonidine–bupivacaine, buprenorphine–bupivacaine and bupivacaine alone in lower limb surgeries. Anaesthesia Essays Res. 2016; 10: 455-61.
14. SoumyaSamal, P. Rani, Chandrasekar LJ and Saubhagya Kumar Jena. Intrathecal buprenorphine or intrathecal dexmedetomidine for postoperative 110 analgesia for lower abdominal and lower limb surgeries.The Health Agenda 2014 Jan;2(1):9-14.
15. Rao BD, Prakash KC.Comparative study of intrathecal bupivacaine 0.5% with bupivacaine 0.5% and buprenorphine low dose for postoperative analgesia in lower abdominal surgeries. Int Surg J 2016;3:253-7