ORIGINAL RESEARCH PAPER
Volume - 12 | Issue - 02 | February - 2023 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

RANDOMIZED COMPARATIVE STUDY OF ANALGESIC EFFICACY OF BUPRENORPHINE AND CLONIDINE AS ADJUVANTS WITH INTRATHECAL BUPIVACAINE IN PATIENTS UNDERGOING TOTAL ABDOMINAL HYSTERECTOMY.

Anesthesiology

Dr Pradeep Kumar Venugopal* 3rd Year Post Graduate, Department of Anesthesia, Sri Siddhartha Medical College and Research Institute, Tumkur. *Corresponding Author

Dr SB Gangadhar Professor and HOD, Department of Anesthesia, Sri Siddhartha Medical College and Research Institute, Tumkur.

Dr Chandana N Assistant Professor, Department of Anesthesia, Sri Siddhartha Medical College and Research Institute, Tumkur.

ABSTRACT

Introduction: Understanding pain and continued efforts to alleviate pain is utmost priority perioperatively. Most often pain is underestimated in all age groups. This study is intended to evaluate and compare analgesic efficacy of two drug combinations with local anesthetic agent in spinal anesthesia. In this study efficacy of Clonidine-Bupivacaine, Buprenorphine-Bupivacaine and Bupivacaine is studied in patients undergoing total abdominal hysterectomy. **Material and Methods:** This study was a prospective randomized study conducted on 114 patients aged 35-60 years who underwent total abdominal hysterectomy at Sri Siddhartha Medical College and Research institute for a period of 24 months.After the approval of institutional ethical clearance committee, 114 ASA I and II patients scheduled for elective total abdominal hysterectomy were selected for study. All the patients were evaluated as per the protocol. The anesthetic procedure was explained to the patients in a simple language and informed consent were obtained. The patients were divided into three groups of 38 each using chit in a box technique. Three groups included Bupivacaine 0.5% hyperbaric (Group B), Clonidine and Bupivacaine 0.5% hyperbaric (Group BC), Buprenorphine and Bupivacaine 0.5% hyperbaric (Group BB). Time of onset of sensory blockade, the height of sensory blockade, motor blockade as per Bromage scale were recorded. Total duration of sensory blockade and motor blockade were also noted. Quality of analgesia (visual analogue score), two segment sensory regression time and time to first rescue analgesia in 24h were documented. **Results:** The total duration of analgesia was statistically significant in all three groups. The mean duration of analgesia was 2.436 ± 0.24h in group B, 2.96 ± 0.32h in group BB and 4.35± 0.62h in group BC. The total duration of motor block was found to be statistically significant between the groups. Mean duration of motor block was 3.10 ± 0.34h in group B , 3.41 ± 0.25h in group BB, 4.48± 0.19h in group BC. The VAS score was found to be statistically significant between the groups. It was 4.68 ± 0.47 in group B, 4.92 ± 1.07 in group BB and 4.42± 0.50 in group BC. **Conclusion:** Clonidine is an effective intrathecal adjuvant to Bupivacaine(H) than Buprenorphine in providing post-operative analgesia and the analgesic efficacy of both Clonidine and Buprenorphine as adjuvants with Bupivacaine(H) were better than Bupivacaine(H) alone.

KEYWORDS

Bupivacaine(H), Clonidine, Buprenorphine, Spinal, total abdominal hysterectomy

INTRODUCTION

Spinal anesthesia is one of the most common techniques used in surgical procedures, whether it is elective or emergency. Especially in cases involving c-sections, gynecological surgery, lower abdominal surgery, orthopedic surgeries et cetera. Although it has the disadvantages of shorter duration of block and less postoperative analgesia, the spinal block is still the method of choice because of its rapid onset, superior blockade, lower risk of infection, lesser failure rates, and cost-effectiveness. When used on their own, local anesthetics are known for having a relatively short duration of action[1]. Intrathecally administered doses of various adjuvants, such as epinephrine, neostigmine, midazolam, ketamine, fentanyl, buprenorphine, clonidine, and dexmedetomidine have shown to improve the quality and duration of spinal anesthesia, also extending analgesia to postoperative period.

A selective agonist for beta 2-adrenoceptors, clonidine is an imidazoline compound that has a selectivity ratio of about 220:1 for beta 2-adrenoceptors over beta 1-adrenoceptors. In 1974, Paalzow was the first person to describe the analgesic effects that can be caused by clonidine[2]. Clonidine administered in the neuraxial region inhibits the release of substance P from the spinal cord as well as the firing of nociceptive neurons brought on by noxious stimulation. In order to exert its analgesic effect, it has to first block the action of cGMP[3]. Clonidine is a beta 2-adrenergic agonist that acts both centrally in the brain stem and peripherally in the body[4]. The hypothalamic 2-adrenoceptors has an inhibiting effect, which leads to a reduction in the amount of outflow from the vasomotor and sympathetic centers. This helps to explain why there was a resultant decrease in peripheral vascular resistance as well as heart rate, blood pressure, and cardiac output. In labor analgesia, gynecological surgery, and orthopedic surgeries, clonidine is used both on its own and in combination with opioids and local anesthetics.

Buprenorphine acts as both an agonist and an antagonist for the mu and kapa opioid receptors. Its action on opioid receptors results in analgesic effects when the drug is administered intrathecally[5]. Buprenorphine is a thebaine derivative, which is a naturally occurring opium alkaloid. It has a potent agonist action at beta opioid receptors and a partial antagonist action, thus preventing addiction or physical dependence. As it is highly lipophilic, doses administered intrathecally are lower and even with lower doses it produces profound and prolonged analgesia. Delayed respiratory depression seen in opioids like morphine is less likely to occur with buprenorphine because it is attached to spinal opioid receptors for a long duration and it spreads through CSF to higher centers. When buprenorphine is used intrathecally as an adjuvant with bupivacaine, it improves both quality and duration of postoperative analgesia in comparison to bupivacaine alone[6].

This study is intended to evaluate and compare two drug combinations with local anesthetic agent in spinal anesthesia ie, clonidine-bupivacaine, buprenorphine-bupivacaine and bupivacaine alone in total abdominal hysterectomy.

MATERIALS AND METHODS:

After obtaining institutional ethical committee clearance, 114 patients aged 35-60 years posted for elective total abdominal hysterectomy under spinal anesthesia were selected for the study. A written informed consent was taken. A detailed history, thorough clinical examination and investigations as per requirements were done.

Inclusion Criteria

- ASA I and II aged 35-60yrs;
- Patients undergoing elective total abdominal hysterectomy surgeries;
- Weight >45kgs
- Height >150cm

Exclusion Criteria:

- ASA Class III or more
- Patients not willing for spinal anesthesia
- Patients with gross spinal deformities
- Patient posted with bleeding diathesis
- Patients with known allergy to test drug
- Patients with a history of any cardiac or respiratory or CNS

disease.
- Patients with hepatic or renal dysfunction,
- Patients with raised intra cranial pressure.

Methods:
All the patients underwent preanesthetic evaluation as per the protocol. The anesthetic and surgical plan was explained to the patients in a simple language and the informed consent was obtained. The patients were divided into three groups of 38 each using chit in a box technique.

PARAMETERS MEASURED
Heart rate (beats/min)
Systolic blood pressure (mmHg)
Diastolic blood pressure (mmHg)
Mean arterial blood pressure (mmHg)
End tidal CO2 (mmHg)

PREPARATION OF PATIENT
Patients were advised to stay nil per oral overnight. All patients were given T.Alprazolam 0.5 mg on the previous night of surgery. On arrival to operating room, IV line was secured, and ringer lactate solution were infused 4–6 ml/kg/h. All patients were monitored with non-invasive blood pressure (BP), electrocardiograph (ECG), pulse oximeter (SpO2). Under all aseptic precautions after putting the patient in left lateral position, using 25-guage Quincke spinal needle, spinal block was performed at lumbar third and fourth interspace through a midline approach and the patient was put to supine position. Patients in Group A received 3ml of 0.5% hyperbaric bupivacaine with 1ml normal saline, Group BB received 3ml of 0.5% hyperbaric bupivacaine with 1ml (60mcg) of buprenorphine (1:5 dilution) and Group BC received 3ml of 0.5% hyperbaric bupivacaine with 1ml (30mcg) clonidine (1:5 dilution).

The time of intrathecal injection was considered as 0. The vital parameters pulse rate, systolic blood pressure, diastolic blood pressure, mean arterial pressure and SpO2 were recorded. Time of onset of sensory blockade, the height of sensory blockade, motor blockade were noted as per Bromage scale, total duration of sensory blockade and motor blockade, quality of analgesia (visual analogue score), two-segment sensory regression time, time to first rescue analgesic, and number of rescue analgesics in 24 h were also monitored. The vital signs were recorded at time 0, 2, 5 min, then every 10 min for first hour and half-hourly until the end of surgery.

RESULT:
Table 1: Table Of Spread Of Analgesia Among The Study Participants (N=114)

Slno	Group	Mean±SD	P
1	Group B	5.68±1.18	0.032
2	Group BB	6.05±1.33	
3	Group BC	6.37±0.75	

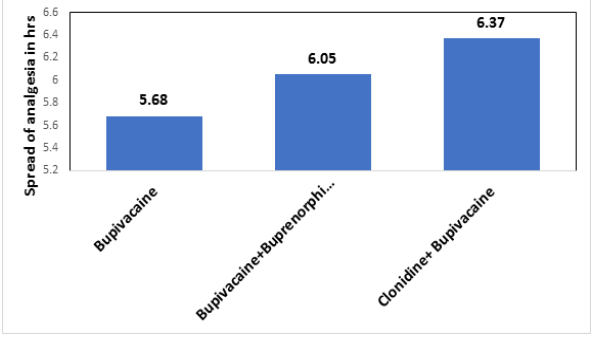


Figure 9: Distribution of spread of analgesia among the study participants (N=114)

Spread of analgesia was statistically less among group BB and group B. Group B 5.68±1.18 hrs, group BB 6.05±1.33 hrs and group BC 6.37±0.75 hrs.

Table 2: Table Of Onset Of Analgesia (in Min) Among The Study Participants (N=114)

Slno	Group	Mean±SD	p
1	Group B	3.29±1.30	<0.001
2	Group BB	4.21±1.98	
3	Group BC	3.79±1.76	

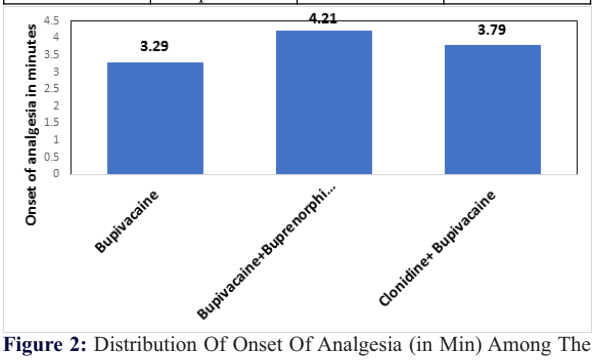


Figure 2: Distribution Of Onset Of Analgesia (in Min) Among The Study Participants (N=114)

Onset of analgesia was statistically high among group BB. Group B 3.29±1.30 min, group BB 4.21±1.98 min and group BC 3.79±1.76 min.

Table 3: Table Of Onset Of Motor Block Among The Study Participants (N=114)

Slno	Group	Mean±SD	P
1	Group B	4.10±1.34	<0.001
2	Group BB	5.89±1.80	
3	Group BC	4.66±1.90	

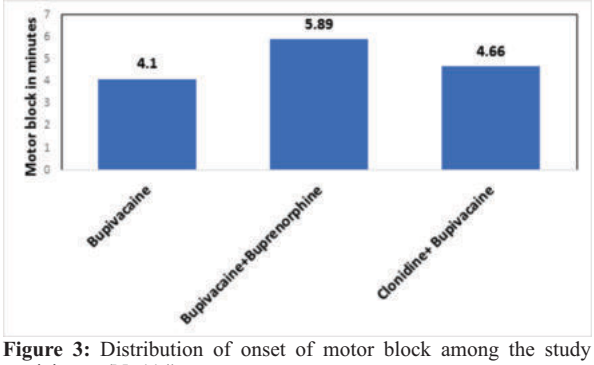
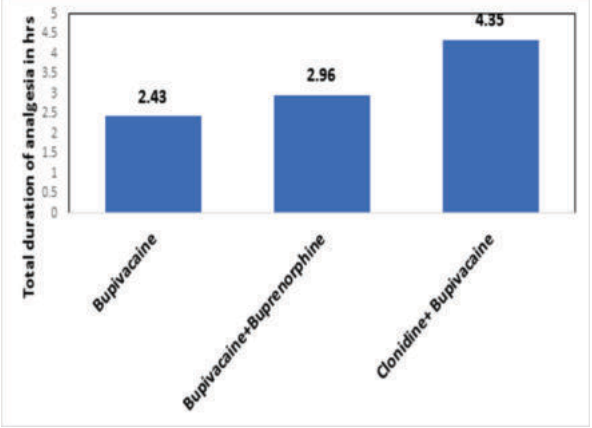


Figure 3: Distribution of onset of motor block among the study participants (N=114)

Onset of motor block was statistically high among group BB. Group B 4.10±1.34 min, group BB 5.89±1.80 min and group BC 4.66±1.90 min.

Table 4: Table Of Total Duration Of Analgesia Among The Study Participants (N=114)

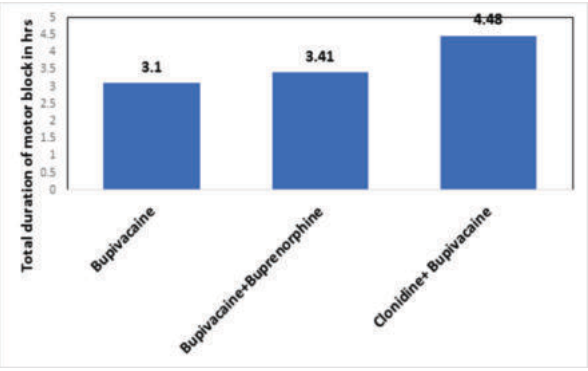
Slno	Group	Mean±SD	p
1	Group B	2.43±0.25	<0.001
2	Group BB	2.96±0.32	
3	Group BC	4.35±0.62	



Duration of analgesia was statistically less among group BB and group B.
Figure 4: Distribution Of Total Duration Of Analgesia Among The Study Participants (N=114)

Table 5: Table Of Total Duration Of Motor Block Among The Study Participants (N=114)

Slno	Group	Mean±SD	p
1	Group B	3.10±0.34	<0.001
2	Group BB	3.41±0.25	
3	Group BC	4.48±0.19	

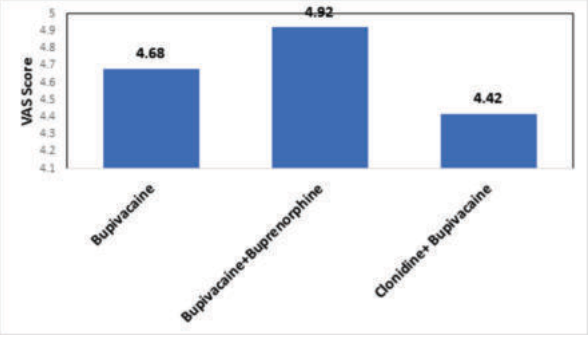


Total duration of motor block was statistically less among group BB and group B. Group B 3.10±0.34 min, group BB 3.41±0.25 min and group BC 4.48±0.19 min.

Figure 5: Distribution of total duration of motor block among the study participants (N=114)

Table 6: Table Of VAS Score Among The Study Participants (N=114)???

Slno	Group	Mean±SD	P
1	Group B	4.68±0.47	0.01
2	Group BB	4.92±1.07	
3	Group BC	4.42±0.50	



Total mean VAS score was statistically less among group BC than group group B and group BB

Figure 6: Distribution of VAS Score among the study participants (N=114)

Table 7: Table Of Side Effects Among The Study Participants (N=114)

	Bupivacaine	Bupivacaine+ Buprenorphine	Clonidine+ Bupivacaine
Bradycardia	0 (0)	0 (0)	2 (5.3)
Chest pain	2 (5.3)	2 (5.3)	0 (0)
Cough	0 (0)	2 (5.3)	0 (0)
Hypotension	0 (0)	0 (0)	1 (2.6)
Nausea	0 (0)	4 (10.5)	3 (7.9)
Vomiting	0 (0)	7 (18.4)	0 (0)

X^2=80.24 (14), p=<0.001

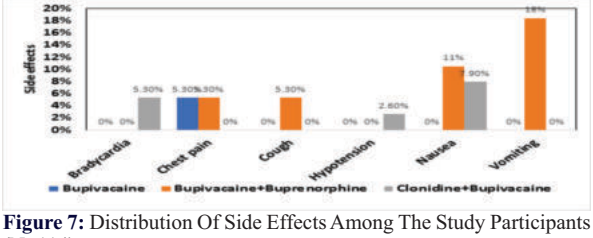


Figure 7: Distribution Of Side Effects Among The Study Participants (N=114)

Side effects were more profound in group BB than group BC and was statistically significant. In group B two reported chest pain. Among group BB, 2 reported chest pain, 2 reported cough, 4 reported nausea and seven reported vomiting. Among group BC 2 reported bradycardia, 1 reported hypotension and three reported nausea.

DISCUSSION

It is considered to be good practice in the field of anesthesia to manage pain during the post-operative period, as well as to provide enough muscle relaxation and analgesia during the intra-operative phase. In order to achieve a more favorable outcome for patients and reduce their risk of morbidity and death, it is critical that the pain that is caused by surgery be managed effectively.

Spinal anesthesia is typically used for lower abdominal procedures because, in comparison to epidural anesthesia and general anesthesia, it is easy to perform and airway related complications are less. However, the most significant drawback of spinal anesthesia is less postoperative analgesia unlike in epidural analgesia as it is a single shot procedure.

This study was conducted to analyze the effect of adjuvants, Clonidine and Buprenorphine with Bupivacaine and to evaluate the duration of postoperative analgesia with each drug and the intraoperative hemodynamic stability in patients undergoing total abdominal hysterectomy.

After pre-anesthetic check-up and getting informed consent, 114 patients of ASA I and II of both sexes, between 35-60 years of age, who were scheduled to undergo total abdominal hysterectomy were included in the study. They were randomly allocated into 3 groups of 38 patients each.

Demographic parameters like Age, sex, height and weight were statistically insignificant among the study subjects.

Spread of analgesia was statistically less among group BB and group B. Group B 5.68±1.18 hrs, group BB 6.05±1.33 hrs and group BC 6.37±0.75hrs.

Onset of analgesia was statistically high among group BB. Group B 3.29±1.30 min, group BB 4.21±1.98 min and group BC 3.79±1.76 min.

Onset of motor block was statistically high among group BB. Group B 4.10±1.34 min, group BB 5.89±1.80 min and group BC 4.66±1.90 min.

Total duration of motor block was statistically less among group BB and group B. Group B 3.10±0.34, group BB 3.41±0.25 and group BC 4.48±0.19.

Total mean VAS score was statistically less among group BC than group group B and group BB.

COMPLICATIONS:

Side effects were more profound in group BB than group BC and was statistically significant. In Group B two reported chest pain. Among group BB 2 reported chest pain, 2 reported cough, 4 reported nausea and seven reported vomiting. Among group BC 2 reported bradycardia, 1 reported hypotension and three reported nausea.

CONCLUSION

The findings of this study concerning the onset time of sensory and motor blockade, the duration of sensory and motor blockade, and post operative analgesia show spinal clonidine has a longer duration of sensory and motor blockade, and it has good post-operative analgesia. The findings suggest that the use of clonidine with bupivacaine in total abdominal hysterectomy has an added advantage in comparison to buprenorphine with bupivacaine and bupivacaine alone, as it provides longer duration of sensory and motor blockade, faster onset time of sensory block and good post-operative analgesia, promotes early ambulation, shorter duration of hospital stay, and thus reduces postoperative morbidity. Additionally, it prevents the simultaneous exposure to multiple drugs and their adverse effects.

FINANCIAL SUPPORT & SPONSORSHIP

No

CONFLICT OF INTEREST:

No conflict of interest

REFERENCES

1. Bafna, U., Yadav, H., & Sharma, N.. COMPARISON OF INTRATHECAL BUPRENORPHINE VERSUS CLONIDINE AS AN ADJUVANT TO 0.5% HYPERBARIC BUPIVACAINE IN LOWER ABDOMINAL SURGERIES. International Journal of Medical and Biomedical Studies. April 2020; 4(4):04-08.
2. Arora R, Pandey V, Sodhi GS, Mohindra B K. A comparative study of intrathecal bupivacaine and bupivacaine with different doses of clonidine in lower limb surgeries. Anesth Essays Res.2018;12:412-6
3. Ahmed F, Khandelwal M, 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 Anesthesia Clin Pharmacol.2017;33:102-6
4. Arora MV, Khan MZ, Choubey MS, Rasheed MA, Sarkar A. Comparison of spinal block after intrathecal clonidine–bupivacaine, buprenorphine–bupivacaine and bupivacaine alone in lower limb surgeries. Anesth Essays Res. 2016;10:455-61.
5. Maharani B, Prakash S M, kalaiah P, elango N C, DEXMEDETOMIDINE AND BUPRENORPHINE AS ADJUVANT TO SPINAL ANAESTHESIA - A COMPARATIVE STUDY. ijcrr. 2013 june; 5(11): 104-110
6. Shilpashri A. M, Roychoudhury P, Girish K. M. "Comparative Study of 0.5% Bupivacaine and 0.5% Bupivacaine with Clonidine (30µg) For Spinal Anaesthesia". Journal of Evolution of Medical and Dental Sciences. 2015 September; 4(71): 12385-12396
7. Singh R, Kundra S, Gupta S, Gupta S, Grewal A, Tewari A. Effecr of clonidine and/or fentanyl in combination with intrathecal bupivacaine for lower limb surgery . J Anaesthesiol Clin Pharmacol.2015;31:485-90
8. Sindhura k, chakravathy K, Krishna B.M, Chaitanya M.M, rupa Y.S. a Comparative Study of Intrathecal 0.5% Bupivacaine and 0.5%Bupivacaine with Clonidine for Lower Abdominal Surgeries IJMSCR. december 2019;07(12):817-822.
9. Kaplan KM, Spivak JM, Bendo JA. Embryology of the spine and associated congenital abnormalities. Spine J. 2005 Sep-Oct;5(5):564-76.
10. Alruwaili AA, M Das J. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Jul 25, 2021. Myelomeningocele.
11. Nasser R, Yadla S, Maltenfort MG, Harrop JS, Anderson DG, Vaccaro AR, Sharan AD, Ratliff JK. Complications in spine surgery. J Neurosurg Spine. 2010 Aug;13(2):144-57.
12. US Preventive Services Task Force. Curry SJ, Krist AH, Owens DK, Barry MJ, Caughey AB, Davidson KW, Doubeni CA, Epling JW, Kemper AR, Kubik M, Landefeld CS, Mangione CM, Phipps MG, Pignone M, Silverstein M, Simon MA, Tseng CW, Wong JB. Screening for Osteoporosis to Prevent Fractures: US Preventive Services Task Force Recommendation Statement. JAMA. 2018 Jun 26;319(24):2521-2531.
13. Dydyk AM, Khan MZ, Singh P. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Oct 3, 2021. Radicular Back Pain.
14. Shamrock AG, Donnally III CJ, Varacallo M. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Aug 9, 2021. Lumbar Spondylolysis And Spondylolisthesis.
15. Viswanathan VK, Subramanian S. StatPearls [Internet]. StatPearls Publishing; Treasure Island (FL): Aug 19, 2021. Pott Disease.