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# Evaluation and comparison of clinical efficacy, post-operative analgesia and hemodynamic effect of intrathecal hyperbaric bupivicaine versus intrathecal hyperbaric bupivicaine plus neostigmine during lower abdominal and lower limb surgeries.

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## ABSTRACT

**Background:** Spinal anaesthesia, which is one of the techniques for infraumbilical surgeries, is most commonly criticized for limited duration of postoperative analgesia. Several adjuvants have been tried along with local anesthetic for prolonging the duration of analgesia.

**Aim and Objective:** To evaluate and compare the post-operative analgesic effect of hyperbaric bupivicaine and hyperbaric bupivicaine plus neostigmine and assess the duration of analgesia, cumulative analgesia and time of rescue analgesia.

**Methodology:** The study was conducted in the Department of Anesthesia, Santosh Medical College and Hospital, Ghaziabad, U.P. from December 2013- july 2014. The patients were randomly assigned to one of the two groups with 30 patients each. Allocation into groups was done by using sealed envelopes. Group A received intrathecally 2.5 ml of 0.5% of

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hyperbaric bupivacaine plus 1ml of normal saline. Control Group B received intrathecally 2.5ml of 0.5% hyperbaric bupivacaine plus 50 mcg of neostigmine (1ml) - Study Group.

**Result:** The mean VAS score in the control group remained zero for 45 minutes after the drug administration, whereas it remained zero for 90 minutes in the study group. The control group's mean VAS score at 180 minutes was 1.03±1.129, while that of the study group was 0.43±0.679 statistically significant was (p value= 0.014).

**Conclusion:** We found that use of intrathecal hyperbaric bupivicaine as adjuvant with the local anesthetic in spinal anaesthesia significantly increases the duration of analgesia (median 320 min versus 220 min) and motor block (median 255 min versus 195 min) but decreases the incidence of postoperative nausea-vomiting (PONV).

**Keywords:** infraumbilical ,surgeries , hyperbaric , bupivacaine ,

## INTRODUCTION

Pain is the most common symptom that brings patients to see a physician. Pain is not just a sensory modality but is an experience. The International Association for the Study of Pain (IASP) [1] defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage or described in terms of such damage. This definition recognizes the interplay between emotional and psychological components. The response to pain can be highly variable among persons as well as in the same person at different times. Pain management especially in the post-operative period is an essential practice in the field of anaesthesiology. Providing purposeful and proper post-operative analgesia has become a popular practice for the sake of patient comfort.

Spinal subarachnoid block is one of the most versatile regional anesthesia techniques available today. Regional anesthesia offers several advantages over general anesthesia-blunts stress response to surgery, decreases intraoperative blood loss, lowers the incidence of postoperative thromboembolic events, and provides analgesia in early postoperative period. Subarachnoid block provides adequate anesthesia for patients undergoing infraumbilical surgery. Among the local anesthetics, 0.5% hyperbaric bupivacaine is the most commonly used drug for spinal anesthesia [2]. The most important disadvantage of single injection SAB is the limited duration. Adjuvants have long been used along with local

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anesthetics to prolong the duration of anesthesia and analgesia. Prolongation of pain relief by various adjuvants like opioids (like morphine [3], fentanyl [4]), ketamine [5], clonidine [6], and neostigmine [7] were investigated by various investigators. However, each drug has its limitations and side effects, and the need for an alternative methods and drugs always exist. Discovery of benzodiazepine receptors in spinal cord in 1977 [8] triggered the use of intrathecal midazolam for prolongation of spinal anesthesia. In vitro autoradiography has shown that there is a high density of benzodiazepine (GABAA) receptors in Lamina II of the dorsal horn in the human spinal cord, suggesting a possible role in pain modulation [9]. So far different animal studies have revealed no damage to the spinal cord, nerve roots, or meninges and in vitro studies.

Karaaslan K, GulcuN, OzturkH, SarpkayaA, Colak C, Kocoglu H 2009 [11] :conducted a study aimed to evaluate the analgesic efficacy duration of analgesia, and side effects of two different doses of caudal neostigmine used with levobupivacaine in children. Sixty boys, between 5 months and 5 years, undergoing genitourinary surgery were allocated randomly to one of three groups (n =20 each). Group I patients received caudal 0.25% levobupivacaine (1 ml/kg(- 1)) alone. Groups II and III patients received neostigmine (2 and 4 mcg/kg(-1) respectively) together with levobupivacaine used in the same does as Group I. They concluded that Caudal neostigmine in doses of 2 and 4 mcg/kg(-1) with levobupivacaine extends the duration of analgesia without increasing the incidence of adverse effects, and 2 mcg/kg(-1) seems to be the optimal dose, as higher dose has no further advantages. Gupta Shobhana in 2010 [12] conducted a study to compare post-operative analgesia and side effects of intrathecal neostigmine with two different doses 75mcg and 50mcg with .5% heavy bupivacaine (15mg).this study concluded that post-operative analgesia is better with 75mcg neostigmine group compared to 50mcg neostigmine group, side effects are also more frequent in 75mcg neostigmine group. HyeMA, MasudKM, BanikD, HaqueMF, Akhtaruzzaman KM in 2010 [13] conducted a study to evaluate post-operative analgesic efficacy and safety of intrathecal neostigmine. This study concluded addition of neostigmine to intrathecal bupivicaine extends the duration of post-operative analgesia with fewer side effects on fetus following caesarean section.[14-17]

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After extensive trials in animals regarding the efficacy and safety, it was testedon human volunteers. After its efficacy and safety was proved in human volunteers, itis being routinely used to provide postoperative analgesia in patients.

## MATERIALS AND METHODS

The study was conducted in the Department of Anesthesia, Santosh Medical College and Hospital, Ghaziabad, U.P. from December 2013- july 2014. The patients were randomly assigned to one of the two groups with 30 patients each. Allocation into groups was done by using sealed envelopes. Group A received intrathecally 2.5 ml of 0.5% of hyperbaric bupivacaine plus 1ml of normal saline. Control Group B received intrathecally 2.5ml of 0.5% hyperbaric bupivacaine plus 50 mcg of neostigmine (1ml) - Study Group.

Anaesthesia technique & recording: The back was thoroughly cleaned with savlon, betadine, and spirit and draped with towels; 1-2 ml of 2% Lignocaine was given with disposable hypodermic needle at L3-L4 intervertebral space which was identified as the space just above or at the junction of line adjoining the highest points of the two iliac crests.[18-20] 23G spinal needle with its bevel parallel to longitudinal dural fibres, was then advanced slowly to heighten the sense of tissue planes traversed and to prevent skewing of nerve roots until the characteristic change in resistance was noted as the needle pass through ligamentum flavum and dura. Correct placement of the tip of the needle into the subarachnoid space was confirmed by the free flow of CSF at the hub of the needle. Drug was injected into the subarachnoid space and the needle was then withdrawn. The patients were then placed in the supine position.

After injecting the drug, sensory and motor blockade were assessed and vital parameters noted. Pulse, non-invasive blood pressure and oxygen saturation were noted at 0 min (at the time of injecting the drug), 1 min, 2 min, 5 min, 10 min, and thereafter every 15 min till the surgery continued. Onset the sensory block, maximum level of sensory block and time of achieving maximum level of sensory block was assessed by pin prick method.

## RESULTS

**Table 1: Demographic data distribution of study subject.**

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| Demographic Distribution | | Number (Percentage) | |
|---|---|---|---|
| | | Study Group | Control Group |
| Age Groups (Years) | 16-25 | 6 (20%) | 6 (20%) |
| | 26-35 | 9 (30%) | 10 |
| | 36-45 | 5 (16.67%) | 6 (20%) |
| | 46-55 | 9 (30%) | 5 (16.67%) |
| | >55 | 1 (3.33%) | 3 (10%) |
| Gender | Male | 20 (66.66%) | 18 (60%) |
| | Female | 10 (33.33%) | 12 (40%) |
| Age | Mean±SD | 37.47 ±10.83 | 38.37±15.01 |
| Weight | Mean±SD | 60.87±7.956 | 59.47±9.895 |

Mean age of patients in Study group was 37.47±10.83 and38.37± 15.05 in control group. The two groups in the present study are comparable in terms of their age distribution. 10(33.33%) females and 20(66.66%) male in study group whereas 12(40%) females and 18(60%) males in the control group. Average weight in study group was 60.87±7.956 and in control group it was 59.47±9.895.

**Table 2: Interoperative pulse rate, SBP, DBP and MAP. (N=30)**

| | Study Group | Control Group | p value |
|---|---|---|---|
| Pulse Rate | 84.70±11.79 | 86.30±11.20 | 0.5920 |
| SBP | 126.27±11.94 | 131.63±11.80 | |
| DBP | 77.57±7.32 | 85.50±8.74 | |
| MAP | 92.97±8.15 | 101.57±8.92 | |

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In Table 2, Intrathecal Neostigmine in the dose of 50µg significantly decreases the onset time of sensory analgesia.The mean heart rate was comparable in both the groups and was found to be statistically insignificant.

**Table 3: Distribution of sensory block onset and time taken to achieve maximum sensory block level, duration of sensory regression to S1 level.**

| | **Time (min)** | **Group** | | **p value** |
|---|---|---|---|---|
| | | Study Group | Control Group | |
| **Sensory Block Onset** | 0-3 | 30 | 25 | p = 0.001 |
| | 4-7 | 0 | 5 | |
| | 8-10 | 0 | 0 | |
| | Mean±SD | 1.48±0.425 | 2.85±0.671 | |
| **Sensory Block Level** | 3-5.5 | 7 | 0 | p = 0.002 |
| | 6-8.5 | 23 | 23 | |
| | 9-15 | 0 | 7 | |
| | Mean±SD | 6.40±1.029 | 7.53±1.167 | |
| **Duration Of Sensory Regression** | 90-139 | 1 | 0 | p = 0.001 |
| | 140-189 | 1 | 6 | |
| | 190-239 | 5 | 17 | |
| | 240-289 | 10 | 7 | |
| | 290-339 | 11 | 0 | |
| | 340-420 | 2 | 0 | |
| | Mean±SD | 272.87±59.52 | 215.13±26.23 | |

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In Table 3 , Mean Time taken to achieve maximum level of sensory block was 6.40±1.029 in study group as compared to 7.53±1.167 in control group. Intrathecal Neostigmine in the dose of 50µg significantly decreases the Mean Time taken to achieve maximum level of sensory block. Maximum level of sensory block achieved was T4 by 8 patients (26.66%) in study group as compared to 12 patients (40%) in control group. The results were statistically not significant and comparable. Duration of sensory regression to S1 level was 215.13±26.23 in Control group as compared to 272.87±59.52 in study group, p value = 0.001 this was significant statistically. The two segment regression of sensory block was significantly prolonged with addition of neostigmine.

**Table 4: Distribution of visual analogue scores and administration time of rescue analgesia.**

| Scores | Time (min) | Group | | p value |
|---|---|---|---|---|
| | | Study Group | Control Group | |
| Visual Analogue Scores | VAS 15 | 0.00±0.00 | 0.00±0.00 | p = 0.014 |
| | VAS 45 | 0.00±0.00 | 0.00±0.00 | |
| | VAS 90 | 0.00±0.00 | 0.03±0.183 | |
| | VAS 180 | 0.43±0.679 | 1.03±1.129 | |
| | VAS 360 | 3.70±1.055 | 4.67±0.959 | |
| Administration Time of Rescue Analgesia | 101-150 | 0 | 0 | p = 0.001 |
| | 151-200 | 0 | 13 | |
| | 201-250 | 0 | 6 | |
| | 251-300 | 6 | 11 | |
| | 301-350 | 6 | 0 | |
| | 351-400 | 13 | 0 | |
| | 401-450 | 5 | 0 | |
| | 451-500 | 0 | 0 | |

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In Table 4, Mean VAS score in the control group remained zero for 45min after administration of the drug as compared to 90min in the study group. Mean VAS score at 180 min was 1.03± 1.129 for the control group as compared to 0.43± 0.679 for the study group. (p value= 0.014) which was significant statistically. The duration of analgesia which was assessed using VAS was observed in both the groups for 24 hours post-operative period. Themean duration of analgesia for control group was 223.80±42.302 min and for study group 462.70± 38.587 min. The statistical analysis showed that the time of duration of analgesia in studygroup was significantly more when compared to control group (p value =0.001).

## DISCUSSION

After taking the informed consent, 60 patients of ASA 1 and ASA 2 were systematically randomized into 2 groups of 30 patients each. Group Areceived intrathecally 2.5 ml of 0.5% of hyperbaric bupivacaine plus 1ml of normal saline. - Control Group. Group B received intrathecally 2.5ml of 0.5% hyperbaric bupivacaine plus 50 mcg of neostigmine (1ml) . The groups were comparable with respect to age, sex, weight and ASA physical status. There was no statistically significant difference in the type & duration of surgery.[21-23] Lignocaine but the post-operative analgesic duration is limited. Other method of prolonging analgesia is using a continuous epiduralanalgesia.

A intrathecal additive to these local anaesthetics forms a reliable andreproducible method of prolonged post operative analgesia. This technique being simple and less cumbersomehas gained a wide acceptability. Commonly used intrathecal additives to local anaesthetics include Opioids,Clonidine, and Neostigmine. Spinal administration of Neostigmine, an acetyl cholinesterase inhibitor, inhibits breakdown of theendogenous neurotransmitter acetylcholine, thereby inducing analgesia, hence it is an another alternative non opioid additive to local anaesthetics which lacks pruritis, respiratory depression, urinary retention, decreased motility of gut as their side effects.

This clearly shows that, intrathecally administered neostigmine, significantly prolongs the duration of analgesia when administered with local anaesthetic agent, thereby reduces the

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post-operative analgesic consumption with a good quality of analgesia which was assessed using the pain score. Grade of motor block according to the Bromage scale in study group was grade 3 in30 patients (100%) & in control groupgrade 3 in 28 patients (93.33%) & grade 2 in 2 patients (6.66%); results were comparable and insignificant statistically. There were no changes in the hemodynamic parameters such as heart rate and blood pressure in either of the groups and was found to be statistically insignificant.[24-25] Nausea and vomiting a minor side effect which was seen in the neostigmine group was controlled by ondansetron or metoclopramide injections.

## CONCLUSION

The conclusions of our present study were as follows - Intrathecal neostigmine in dose of 50µg can be used along with bupivacaine to provide safe, durable and predictable post-operative analgesia with minimal adverse effects in patients posted for lower abdominal, gynaecological and perineal surgeries , Intrathecal Neostigmine in the dose of 50µg significantly decreases the onset time of sensory analgesia and motor blockade , The duration and quality of post-operative analgesia following intrathecal administration of neostigmine was found to be statistically significant, thereby suggesting that 50µg of intrathecal neostigmine along with bupivacaine provided good post-operativeanalgesia. The requirement of rescue analgesia is reduced in neostigmine group , Intrathecal neostigmine in 50µg dose produces minimal nausea and vomiting which can be easily controlled with antiemetic such as ondansetron or metoclopramide, In the dose of 50µg Neostigmine use intrathecally is not associated with any significant hemodynamic disturbance or respiratory depression.

We conclude that the addition of 2 mg preservative free midazolam to 0.5% hyperbaric bupivacaine for subarachnoid block in infraumbilical surgery prolongs the duration of effective analgesia as compared to bupivacaine alone and delays the need for postoperative rescue analgesics without having any sedative effect, pruritus, or respiratory depression. The use of intrathecal midazolam also decreases the incidence of post-operative nausea-vomiting (PONV). Intrathecal midazolam in a dose of 2 mg does not have any clinically significant effect on perioperative hemodynamics.

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In conclusion, 50mcg neostigmine seems to be an attractive alternative as an adjuvant to spinal bupivacaine in surgical procedures. Significant prolongation of analgesia & adequate motor relaxation without any side effects gives a safe edge in situations where there is unexpected prolongation of surgical procedure.

## REFERENCES

[1] G. E. Morgan Jr., M. S. Mikhail, M. J. Murray, and C. P. Larson Jr., Clinical Anaesthesiology, Lange, New York, NY, USA, 4th edition, 2002.

[2] P. H. Tan, Y. Y. Chia, Y. Lo, K. Liu, L. C. Yang, and T. H. Lee, "Intrathecal bupivacaine with morphine or neostigmine for postoperative analgesia after total knee replacement surgery," Canadian Journal of Anesthesia, vol. 48, no. 6, pp. 551–556, 2001.

[3] C. O. Hunt, J. S. Naulty, A. M. Badder et al., "Peri operative analgesia with subarachnoid fentanyl-bupivacaine for caesarian section," Anaesthesiology, vol. 71, no. 4, pp. 535–540, 1989.

[4] S. Karthival, SdhasivamS, A. Saxena, T. R. Kannah, and P. Ganjoop, "Effects of intrathecal ketamine added to bupivacaine for spinal anesthesia," Anarsthesia, vol. 55, no. 9, pp. 899–904, 2001.

[5] DobrydjnovI, K. Axelsson, J. Samarutel, and B. Holmstrom, "Post operative pain relief following intrathecal bupivcaine with intrathecal or oral clonidine,"Acta Anaesthesiologica Scandinavica, vol. 46, no. 7, pp. 806–814, 2002.

[6] S. Liu, "Dose-response effects of spinal neostigmine added to bupivacaine spinal anesthesia in volunteers," Anesthesiology, vol. 90, no. 3, pp. 710–717, 1999.

[7] H. Mohler and T. Okada, "Benzodiazepine receptor: demonstration in the central nervous system," Science, vol. 198, no. 4319, pp. 849–851, 1977.

[8] R. L. M. Faull and J. W. Villiger, "Benzodiazepine receptors in the human spinal cord: a detailed anatomical and pharmacological study," Neuroscience, vol. 17, no. 3, pp. 791–802, 1986.

ISSN PRINT 2319 1775 Online 2320 7876

*Research paper*  UGC CARE Listed ( Group -I) Journal Volume 11,Iss 7, Oct 2022

[9] Merskey H. Pain terms: A list with definitions and a note on usage. Recommended by the International Association for the Study of Pain (IASP) Subcommittee on Taxonomy.Pain 1979; 6:249-252.

[10] NaguibM,Yaksh TL. Antinociceptive effects of spinal cholinesterase inhibition and isobolographic analysis of the interaction with μ & α2 receptor systems.Anaesthesiology 1994; 80:1338-48.

[11] LaurettiGR, Reis MP, Prado WA, Klamt JG: Dose-response study of intrathecal morphine versus intrathecal neostigmine, their combination, or placebo for postoperative analgesia in patients undergoing anterior and posterior vaginoplasty and posterior vaginoplasty.AnesthAnalg1996;82:1182-1187.

[12] Gabriela R. Lauretti, MD, MSc, PhD, and Vera M. S. Azevedo, MD:Conducted a study to determine whether intravenous (IV) ketamine would enhance analgesia from intrathecal (IT) neostigmine compared with combining IV fentanyl with IT neostigmineAnesthAnalg1996;83:766-70.

[13] Lauretti GR, Mattos AL, Reis MP, Prado WA: conducted a study to establish a dose-response curve for the analgesic effect of intrathecal neostigmine in patients undergoing below knee surgery with spinal anaesthesia.Journal of Clinical Anesthesia 1997;9:473-477.

[14] Krukowski JA, Hood DD, Mallak KA, Eisenach JC and Parker RL Conducted a dose response study of intrathecal neostigmine for post caesarean section analgesiaAnesthAnalg 1997; 84:1269-75.

[15] Klamt JG, SlullitelA, Garcia V and Prado WA : studied post operative analgesic effect of intrathecal neostigmine and its effects on spinal anaesthesia.Anesthesia 1997;52:547-551.

[16] Lauretti GR1, Reis MP: Conducted a study to evaluate the efficacy of operatively administered spinal neostigmine to provide analgesia and that of different antiemetic's to prevent neostigmine-related nausea and vomiting,in patients undergoing tibia or ankle reconstruction. Reg Anaesthesia .1997;22:337-42.

ISSN PRINT 2319 1775 Online 2320 7876

*Research paper*  UGC CARE Listed ( Group -I) Journal Volume 11,Iss 7, Oct 2022

[17] Pan PM1, Huang CT, Wei TT, Mok MS: Enhancement of analgesic effect of intrathecal neostigmine and clonidine on bupivicaine spinal anesthesia. RegAnesth Pain Med.1998;23:49-56.

[18] Liu SS, Hodgson PS, Moore JM, TrautmanWJ,Burkhead DL:Dose responseeffects of spinal neostigmine to bupivacaine spinal Anaesthesia in volunteers.Anesthesiology 1999;90:710-715.

[19] Morgan GE, Mikhail MS, Murray MJ. Clinical Anaesthesiology.4th Edition.Langeand Mc Graw Hill publishers (United states of America): 2006;38:231-234.

[20] Goodman and Gilman. The pharmacological basis of therapeutics.11th Edition.Mc Graw Hill publishing division (United states of America): 2006, 204-214.

[21] Scott.S. Reuben et al, Multimodal analgesia, the journal of bone and joint surgery (American) 2007;89:1343-1358.

[22] AzimHonarmand,Mohammad Reza Safavi Mohammad Reza Habibzadeh: Postoperative analgesic and adverse effects of two low doses of intrathecal neostigmine and its influence on spinal bupivacaine anaesthesia after knee arthroscopy. Acute Pain 2009;11:31–37.

[23] HyeMA,MasudKM,BanikD,HaqueMF,Akhtaruzzaman KM. Intrathecal neostigmine for post-operative analgesia in caesarean section . Mymensingh Med J.2010;19:586-593.

[24] Christian C. Apfel.Acute postoperative pain.Anesthesia. Ronald D. Miller. 7thEdition. USA: Churchill Livingstone: 2010;2729-2756.

[25] Dadu S, Mishra LS, Agrawal M, Chandola HC: Comparative clinical study of effect of neostigmine and ketamine for postoperative analgesia. J Indian Med Assoc.2011;109:308-311