

COMPARISON OF ANALGESIA BETWEEN NEOSTIGMINE AND TRAMADOL ADDED AS ADJUNCT TO 0.125 % BUPIVACAINE IN POSTOPERATIVE EPIDURAL ANALGESIA FOR BELOW UMBILICAL SURGERIES

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Abstract

Background: To observe the post-operative analgesia of neostigmine and tramadol in combination with bupivacaine in the post-operative period after below umbilical surgeries in order to reduce local anesthetic consumption. **Materials and Methods:** After pre-operative epidural catheterisation, the patients were operated under regional anesthesia Total 60 adult patient divided into 3 groups: Group B (receive 0.125% bupivacaine), Group N (receive 0.125% bupivacaine & neostigmine 0.005mg/kg), Group T receive 0.125% bupivacaine & tramadol 1mg/kg. **Result:** Sixty (60) patients were enrolled in this study and 57 patients were subjected to statistical analysis. Overall 24-h visual analog score in group N was significantly less than in those who received Bupivacaine alone ($P = 0.00$) and Bupivacaine with Tramadol. The durations of complete analgesia and effective analgesia were longer for all patients in group N compared with group T ($P < 0.05$) and group B ($P < 0.005$) patients. The total number of epidural top ups (rescue analgesia) required was less in group T ($P < 0.05$) and group N ($P < 0.005$) patients, compared with the control group. The incidence of nausea and vomiting was not increased in group N patients. **Conclusion:** Neostigmine and Tramadol, when used as an epidural analgesia in combination with 0.125% bupivacaine not only increases the analgesia quality but also patient's satisfaction without having any side effects in postoperative period.

INTRODUCTION

To observe the post-operative analgesia of neostigmine and tramadol in combination with bupivacaine in the postoperative period after below umbilical surgeries in order to reduce local anesthetic consumption. The addition of an opioid to epidural local anesthetic Agent needed for analgesia, Minimizes side effects from local anesthetic blockade. However these opioids administered via epidural analgesia can produce side effects themselves, which includes pruritus, etc, for these reasons there has been increase in use of non-opioid adjuvants to reduce epidural local anesthetic agent dose as well as side effects of opioids.^[1,2]

Neostigmine (cholinesterase inhibitor), produces analgesia when given epidurally as it increases acetylcholine stimulation of spinal muscarinic and

to some extent nicotinic receptors. neostigmine produces analgesic effects when given as an Intrathecal injection. The inhibition of spinal cholinesterase by neostigmine leads to increase in endogenous acetylcholine, which is released from intrinsic cholinergic neurons present within the dorsal horn of the spinal cord. These intrinsic cholinergic neurons terminate in the vicinity of primary afferent express muscarinic receptors. The endogenous acetylcholine produces analgesic effect via muscarinic presynaptic inhibition of glutamatergic afferents, similar to how it has been described in the neostigmine.^[3]

Studies of intrathecally administered neostigmine in the mid to late 1990s demonstrated analgesic efficacy and lack of neurological injuries but also dose-dependent, severe nausea and vomiting, and further clinical development on this was abandoned.

In contrast, epidural administration of neostigmine has been shown to reduce local anesthetic requirements in the postoperative setting without nausea and vomiting in both adults and children, Epidural neostigmine also shown to reduce epidural local anesthetic requirement for labor analgesia to a degree similar to that of opioids in small, single-dose studies, including a study in which epidural analgesia is used. In contrast to opioids, there are no large randomized controlled studies evaluating the effects of epidurally administered neostigmine as an adjunct to local anesthetics in below umbilical surgeries. The purpose of the current study was to compare the effects of epidurally administered neostigmine & Tramadol with that of a commonly used concentration when added to 0.125 % bupivacaine during below umbilical surgeries. We hypothesized that epidurally administered bupivacaine combined with neostigmine would reduce total hourly bupivacaine use compared with epidurally administered bupivacaine combined with Tramadol or bupivacaine used alone for below umbilical surgeries analgesia.^[4,5]

MATERIALS AND METHODS

Sixty (60) adult ASA grade I-II patients, aged 18-60 years were taken & divided into three equal groups of 20 patients each. The study took place in LN medical college and J.K. Hospital, Bhopal. After pre-operative epidural catheterization, the patients were operated under regional anesthesia. After surgery, the patients were randomly allocated in a double-blinded manner and divided into three equal groups: Group B: 0.125 % bupivacaine, Group N: 0.125 % bupivacaine along with neostigmine 4 mcg/kg and Group T: 0.125 % bupivacaine along with 1 mg/ kg Tramadol solution. During the following 24 hours, hemodynamic parameters, pain using visual analog scale, total analgesic consumption, additional analgesic requirement, patients satisfaction, and probable side-effects were evaluated.

Type and design of study- Observational Comparative Study

Location – L.N medical college & j.k hospital, in January 2021-July 2022, Approval from IEC. Total 60 adult patient divided into three equal groups:- Group B (will receive 0.125 % bupivacaine), Group N (will receive 0.125 % bupivacaine & neostigmine 0.005mg/kg), Group T will receive 0.125 % bupivacaine & tramadol 1mg / kg.

Inclusion Criteria

ASA Grading, I-II, age 18-60 years, below umbilical surgeries

Exclusion Criteria

ASA Grading III-IV, ages above 60 year, & any comorbidity.

Parameters Evaluated

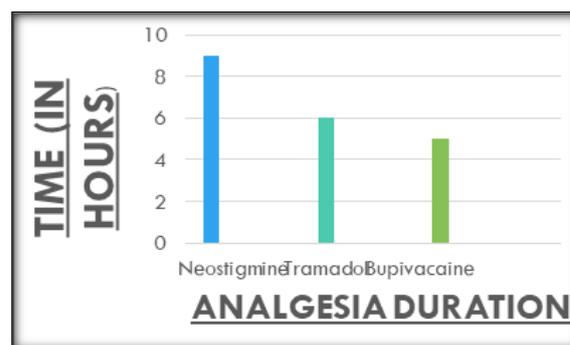
Hemodynamic parameters, visual analogue scale, total analgesic consumption within 24 hours, patient satisfaction LEVEL, & ANY side effects.

Statistical Analysis

Data was compiled in excel sheet and by using spss software 3 version it was analyzed for relevant outcome and p value was considered significant when it was less than 0.05%. Anova test was applied in different variable to see the level of significance.

RESULTS

Sixty (60) patients were enrolled for this study and 57 patients were subjected to statistical analysis. Overall 24-hour visual analog score in group N was significantly less than the group of patients who received Bupivacaine alone (P = 0.00) and Bupivacaine with Tramadol. The duration of complete analgesia and effective analgesia were longer for all patients included in group N compared with group T patients (P < 0.05) and group B (P < 0.005) patients. The total number of epidural top up (i.e. rescue analgesia) required was less in group T patients (P < 0.05) and group N (P < 0.005) patients, when compared with the control group. There was no increase in incidence of nausea and vomiting in group N patients.



Mean Analgesia Duration

Mean analgesic time Group N> Group T> Group B
Visual analogue scale Group N< Group T< Group B

Table 1: Visual Analogue Score

| Visual Analogue score (in hours) | Neostigmine | Tramadol | Bupivacaine |
|----------------------------------|-------------|----------|-------------|
| 1st hour | 0 | 0 | 0 |
| 2nd hour | 0 | 0 | 0 |
| 3rd hour | 0 | 0 | 0 |
| 4th hour | 0 | 0 | 2 |
| 5th hour | 0 | 0 | 3 |

| | | | |
|-----------|---|---|---|
| 6th hour | 0 | 2 | 6 |
| 7th hour | 0 | 4 | 8 |
| 8th hour | 0 | 6 | 8 |
| 9th hour | 0 | 8 | 8 |
| 10th hour | 2 | 8 | 8 |

Table 2: Side Effects

| Serial Number | Neostigmine (Out of 20 patients) | Tramadol (Out of 20 patients) | Bupivacaine (Out of 20 patients) |
|------------------------|-------------------------------------|----------------------------------|-------------------------------------|
| 1. Nausea and Vomiting | 0 | 4 | 1 |
| 2. Headache | 1 | 0 | 0 |
| 3. Shivering | 1 | 0 | 3 |
| 4. Abdominal Pain | --- | --- | --- |

DISCUSSION

In our study, Sixty (60) adult ASA grade I-II patients, aged 18-60 years were taken & divided randomly into three equal groups of 20 patients each. The study aimed to compare the effects as well as adverse effects of Intra Thecal 0.125% bupivacaine, tramadol and neostigmine as adjunct in below umbilical surgeries. We observed that Mean analgesic time for neostigmine is longer as compared to tramadol and bupivacaine and tramadol as compared to bupivacaine alone in post op analgesia.^[6,7]

Explained role of adjuncts in epidural analgesia when given with 0.125% bupivacaine in their study “analgesic effect of intrathecal tramadol as a spinal adjunct to 0.5% heavy bupivacaine in lower abdominal surgeries.”^[4]

Visual Analogue Score is less in neostigmine. Significant reduction in local anaesthetics and analgesics in postoperative period is seen because longer duration of action for neostigmine as compared to tramadol and bupivacaine. Longer duration of action results in less frequent top ups. Lauretti GR de oliveria R et al. Found that Epidural neostigmine in lidocaine produced an analgesic effect which was dose independent compared to the control group and a reduction in postoperative epidural top up without increasing the incidence of adverse effects which was similar to our findings.^[8]

Total analgesic consumption within 24 hours is less while using neostigmine and side effects is also very less. Jessica L. booth et al. Found that epidural opioid are having more side effects as compared to epidural neostigmine in their study “epidural neostigmine vs fentanyl to decrease bupivacaine use in patient controlled epidural analgesia during labour.”^[3] Which was similar to our findings/study.

K.M.HO. Et.al. Used intrathecal Neostigmine as an adjunct for post-operative analgesia in their study, “use of intrathecal Neostigmine as an adjunct to other spinal medication in perioperative period and peripartum analgesia” which was similar to our findings /study.^[5]

Masayasu Nakayama et al, Epidurally administered neostigmine of 10 µg/kg in bupivacaine provides a longer duration of analgesia than bupivacaine alone or when combined with 5 µg/kg of neostigmine after

total abdominal hysterectomy which was similar to our study.^[9]

Rajesh Mahajan et al, Explained that Caudal neostigmine with bupivacaine produces an analgesic effect in children which was dose dependent as compared to those receiving caudal bupivacaine alone and a reduction in post-operative epidural top up without increasing the incidence of adverse effects in their study “caudal neostigmine with bupivacaine produces a dose-independent analgesic effect in children, which is similar to our findings.”^[10]

As compared to previous study, Liu SS, Hodgson PS, Moore JM, Trautman WJ, Burkhead DL 1999; 90 (3): 710 – 7.^[2] They have taken gynaec patient but in our study we have taken patient randomly.

CONCLUSION

Neostigmine and Tramadol, when used as an epidural analgesia in combination with 0.125% bupivacaine not only increases the analgesia quality but also patients satisfaction without having any side effects in postoperative period.

REFERENCES

- Johansen A, Romundstad L, Nielsen CS, Schirmer H, Stubhaug A. Persistent postsurgical pain in a general population: prevalence and predictors in the Tromsø study. *Pain*. 2012;153(7):1390-1396. doi: 10.1016/j.pain.2012.02.018.
- Liu SS, Hodgson PS, Moore JM, Trautman WJ, Burkhead DL. Dose-response effects of spinal neostigmine added to bupivacaine spinal anesthesia in volunteers. *Anesthesiology*. 1999;90(3):710-7. doi: 10.1097/0000542-199903000-00012.
- Booth JL, Ross VH, Nelson KE, Harris L, Eisenach JC, Pan PH. Epidural Neostigmine versus Fentanyl to Decrease Bupivacaine Use in Patient-controlled Epidural Analgesia during Labor: A Randomized, Double-blind, Controlled Study. *Anesthesiology*. 2017;127(1):50-57. doi: 10.1097/ALN.0000000000001669.
- Swain A, Nag DS, Sahu S, Samaddar DP. Adjuvants to local anesthetics: Current understanding and future trends. *World J Clin Cases*. 2017;5(8):307-323. doi: 10.12998/wjcc.v5.i8.307.
- Ho KM, Ismail H, Lee KC, Branch R. Use of intrathecal neostigmine as an adjunct to other spinal medications in perioperative and peripartum analgesia: a meta-analysis. *Anaesth Intensive Care*. 2005;33(1):41-53. doi: 10.1177/0310057X0503300107.
- Booth JL, Ross VH, Nelson KE, Harris L, Eisenach JC, Pan PH. Epidural Neostigmine versus Fentanyl to Decrease

- Bupivacaine Use in Patient-controlled Epidural Analgesia during Labor: A Randomized, Double-blind, Controlled Study. *Anesthesiology*. 2017;127(1):50-57. doi: 10.1097/ALN.0000000000001669.
7. Isbister WH, Bonifant J. Implementation of the World Health Organization 'analgesic ladder' in Saudi Arabia. *Palliat Med*. 2001;15(2):135-40. doi: 10.1191/026921601677212495.
 8. Lauretti GR, de Oliveira R, Reis MP, Julião MC, Pereira NL. Study of three different doses of epidural neostigmine coadministered with lidocaine for postoperative analgesia. *Anesthesiology*. 1999;90(6):1534-8. doi: 10.1097/00000542-199906000-00006.
 9. Nakayama M, Ichinose H, Nakabayashi K, Satoh O, Yamamoto S, Namiki A. Analgesic effect of epidural neostigmine after abdominal hysterectomy. *J Clin Anesth*. 2001;13(2):86-9. doi: 10.1016/s0952-8180(01)00218-5.
 10. Mahajan R, Grover VK, Chari P. Caudal neostigmine with bupivacaine produces a dose-independent analgesic effect in children. *Can J Anaesth*. 2004;51(7):702-6. doi: 10.1007/BF03018429.