ORIGINAL RESEARCH PAPER

Volume-8 | Issue-2 | February-2019 | PRINT ISSN No 2277 - 8179

INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

A COMPARATIVE STUDY OF ANALGESIC EFFECT OF INTRATHECAL NEOSTIGMINE, FENTANYL AND COMBINATION OF BOTH AS AN ADJUVANT TO INTRATHECAL BUPIVACAINE AND BUPIVACAINE ALONE FOR ABDOMINAL HYSTRECTOMY

Anaesthesiology

Dr. Jigyasa Shahani M.D, Assistant Professor Department of Anesthesia Government Medical College

Dr. Fareed Ahmed* M.D, Senior Professor Department of Anesthesia SawaiManSingh Medical College Jaipur. Rajasthan *Corresponding Author

ABSTRACT

Many options are available for post-operative analgesia including systemic analgesics and regional techniques. The aim of this study was to compare analgesic duration of combination of fentanyl and neostigmine with intrathecal bupivacaine, fentanyl and neostgmine alone with intrathecal bupivacaine.

METHOD: 164 patients of ASA grade I and II, scheduled for elective Total Abdominal Hysterectomy under subarachnoid block were randomly allocated to four groups (n=41): Group A received 15mg bupivacaine intrathecally.Group B received 15mg bupivacaine plus 25 micrograms of fentanyl intrathecally.Group C received 15mg bupivacaine plus 25 micrograms neostigmine intrathecally.Group D received 15mg bupivacaine plus 25 micrograms neostigmine and 25 micrograms fentanyl intrathecally with total volume made upto 4.0ml with NS in each group.

RESULT: Duration of analgesia in post operative period was group A (126.05±19.33 minutes),group B (208.2±15.74 minutes),group C (194.37±15.54 minutes),group D (290.8±20.24 minutes.

CONCLUSION: The combination of intrathecal neostigmine and fentanyl with bupivacaine significantly prolonged post operative analgesia as compared to other three study groups.

KEYWORDS

Fentanyl, Neostigmine,Postoperative analgesia

INTRODUCTION

Pain is an unpleasant sensory and emotional experience associated with actual or potential tissue damage. Relief of pain during surgery is the main aim of anesthesia. Any expertise acquired in this field should be extended into post operative period. Many options are available for the treatment of post-operative pain, including systemic analgesics and regional techniques.Neuraxial and peripheral techniques can provide superior analgesia compared to systemic drugs. The cholinergic pathway plays an important inhibitory pathway for pain modulation. Cholinomimetic drugs, including cholinergic receptor agonist and acetylcholinesterase inhibitor known to produce analgesia in various species. Neostigmine is a reversible acetylcholinesrase inhibitor quaternary ammonium compound used as cholinomimetic analgesic in human.

The primary goal of this study was to determine whether the combination of fentanyl and neostigmine with intrathecal bupivacaine has better analgesic duration than fentanyl and neostgmine alone with intrathecal bupivacaine.

METHOD

After approval of the Institutional Ethical Committee and obtaining written informed consent 164 patients of ASA physical status grade I and II, aged 30-50 years, scheduled for elective Total Abdominal Hysterectomy under subarachnoid block were randomly allocated to four groups (*n*=41).**Group A**: Patients received 15mg bupivacaine intrathecally.**Group B**: Patients received 15mg bupivacaine plus 25 micrograms of fentanyl intrathecally . **Group C**: Patients received 15mg bupivacaine plus 25 micrograms neostigmine intrathecally . **Group D**: Patients received 15mg bupivacaine plus 25 micrograms neostigmine and 25 micrograms fentanyl intrathecally with total volume made upto 4.0ml with NS in each group. Exclusion criteria included refusal for consent, ASA Grade III and IV,any deformity or local sepsis in spinal lumbar region,severe hypovolemia, increased intracranial pressure,any coagulation abnormalities, any major pre-existing neurological, cardiovascular, metabolic, hepatic, respiratory or renal disease,history of allergy or hypersensitivity to any of the study drugs and patients in whom spinal anaesthesia failed.

All patients were fasted for at least 6hrs before the procedure.All routine monitors were attached and preoperative baseline readings of blood pressure, pulse rate and saturation were noted. After securing an IV access using 18G intravenous cannula all patients irrespective of the group they belonged were preloaded with Ringer's Lactate 15ml/kg over 10mins. Under all aseptic precautions spinal anesthesia was performed in the operating room at the $L_3 - L_4$ interspace, with the patient in the left lateral position using 25G Quincke spinal needle . A volume of 4.0 ml of drug was injected over 30 seconds without barbotage. The intrathecal drugs composition depended upon the group to which patient belonged. Patient was placed in supine position with a 15° head down tilt immediately after spinal injection to achieve level of block of T5-T6. An indwelling urinary catheter was inserted before the start of the operation. Intraoperative fluid management was done according to the blood loss and hemodynamic parameters. The drug combination was prepared by one anesthesiologist and was given by another experienced one who was blinded to the study drug used and did not take further part in the study. Both patients and the observer were blinded regarding the study drug or group.Sensory block was assessed by the pinprick method bilaterally along the mid-clavicular line with a 25-gauge hypodermic needle at 2 min interval till the highest level of block was achieved and the required time was noted. The onset of sensory block was defined as the time from intrathecal injection of the study drug to the time taken to achieve T6 dermatomal level of sensory block. Regression of sensory block was defined as the time taken for the sensory block to regress by two dermatomal segments from the highest level achieved. Motor block was assessed according to the modified Bromage scale.The onset of motor block was defined as the time from intrathecal injection of the study drug to the time taken to achieve complete motor block (Bromage score-IV). Duration of motor block was the time elapsed from the maximum to the lowest Bromage score I–IV. Intraoperatively, monitoring of blood pressure, pulse rate, saturation and respiratory rate were done at 5 min interval. Hypotension was defined as a fall of mean arterial pressure (MAP) by more than 20% from baseline or a fall of systolic blood pressure below 90 mmHg and it was treated with incremental IV doses of mephentermine 5 mg and IV fluid as required. Bradycardia, defined as HR <50 bpm, was treated with injection atropine 0.6 mg IV. The post-operative pain and sedation level were assessed according to the VAS (0-10) and the 'four point sedation scale' (score 1 = spontaneous eye opening [awake and alert]; score 2 = drowsy, responsive to verbal stimuli; score 3 = drowsy, arousable to physical stimuli; score 4 = unresponsive), respectively, at 30-min interval upto 4 h and hourly thereafter till the request for first rescue analgesia.[5] Every patient received injection diclofenac 75 mg IV as rescue analgesic on VAS of 3. The time from intrathecal injection to first rescue analgesia (total duration of analgesia) was recorded and this was the end point of our study. We observed all patients for next 24 h regarding any complications such as nausea, vomiting, hypotension, bradycardia, respiratory depression and managed them accordingly.

Statistical analysis was performed with the SPSS, version 15.0 for Windows statistical software package (SPSS inc., Chicago, il, USA).

Chi square test, analysis of variance (ANOVA) and student's t-test were used. The level of significance was set at 0.05.

RESULTS

All the groups were comparable with respect to age, weight, ASA status, type of surgery and duration of surgery.

Table 1: CHARACTERISTICS OF SPINAL BLOCK

Variables	Group A	Group B	Group C	Group D
Number of patients	41	41	41	41
Onset of motor block@ (mins)*	8.85±1.24	8.44±1..05	8.46±0.50	8.46±0.71
Total duration of Motor Block$ (mins.)	114±10.07	121±13.52	115±6.62	126±6.1
Time for 2 segment regression (mins) %	79±11.64	125±19.57	125±7.85	135±8.24
Total duration of Analgesia (mins)#	126.05±19.33	208.2±15.74	194.37±15.54	290.8±20.24
Total no.of analgesia dose in 24 hours	3.51±0.51	2.39±0.49	2.54±0.50	1.76±0.49
hours				

@Bromage Grade III; $ Return to Bromage Grade II
* P > 0.05 (Non-Significant)
% Statistically significant difference between: group A was compared with group B (p=0.00), group C (p=0.0000) & group D (p=0.000).

Statistically significant difference between when group A was compared with group B (p=0.00), group C (p=0.000) & group D (p=0.000)

FIGURE 1: COMPARISON OF TIME TO FIRST RESCUE ANALGESIA

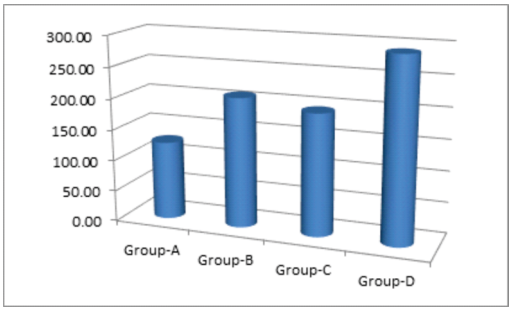

Table 2: INCIDENCE OF ADVERSE EFFECTS

EFFECTS	GROUP A n(%)	GROUP B n(%)	GROUP C n(%)	GROUP D n(%)
Hypotension≠ (*p=0.0937*)	2(4.8%)	5(12.2%)	7(17%)	11(26.8)
Bradycardia≠ (p=0.09302)	2 (4.8%)	1(2.4%)	2 (4.8%)	2 (4.8%)
Respiratory depression≠ *(p=1.00)*	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Nausea, Vomiting≠ (p =0.4284)	2 (4.8%)	3(7.3%)	6(14.6%)	5(12.2%)
Pruritus≠ (*p* >0.05)	0 (0%)	3 (7.3%)	0(0%)	3(7.3%)

DISCUSSION

It is well recognized that the post operative pain is being under treated and the conventional therapy of providing intermittent analgesics on patient demand is an ineffective method of pain relief. The pre-emptive mixing of analgesics with local anaesthetics for regional anaesthesia provides a better alternative. Intrathecal neostigmine causes dose dependent post operative analgesia by inhibiting the breakdown of acetylcholine in dorsal horn and spinal meninges and further, acetylcholine may cause analgesia through direct action on spinal cholinergic muscarinic receptors M1 and M2 and indirectly through stimulation of release of the second messenger nitric oxide in the spinal cord , whose mechanism of action is likely to include activation of second messengers such as cyclic guanosine monophosphate (cGMP)[1].

Our result coincide with **Lauretti et al**[2] in which the total duration of analgesia in combination group of neostigmine and fentanyl was 338 minutes. The total duration of analgesia in fentanyl group was comparable with **Diana F Gabinsky et. Al**[3] in which the total duration of analgesia was 222±13.8 min. It is more as compared to **Biswas B N et al**[4] (183 ± 9 min)who used fentanyl 12.5 micrograms intrathecally However it is less than **Fareed ahmed 2010 et. Al**[5] (249.3±31.06)**.** The total duration of analgesia in Group C is comparable with results of **Shobhana gupta**[6] (183.9±3.36 min)who used neostigmine 50µg with hyperbaric bupivacaine.

In our study the **time for 2 segment regression** was 79 minutes and 135 minutes in Bupivacaine alone Group and Bupivacaine – neostigmine– Fentanyl Group respectively**.** The 2 segment regression time in Group B was 125±19.57 min which is greater as compared to results of **Harbhej Singh et al**[7](93 ± 22 minutes).

In our study the time for The **onset of motor block** was 8.85±1.24 minutes, 8.44±1.05 minutes , 8.46±0.50 minutes , 8.46±0.71 minutes in Groups A,B,C and D respectively. There was no statistically significant difference among the study groups (p>0.05). Our study result coincides with **Harbhej Singh et al**[7] , **Diana F Gabinsky et. Al**[3] **and U Srivastava et al**[8]**.**

In our study The **duration of motor block** was 114±10.07 minutes, 121±13.52 minutes, 115±6.62 minutes and 126±6.1minutes in Groups A,B,C and D respectively. . There was no statistically significant difference among the groups (p>0.05). Our result were comparable with study done by **Harbhej Singh et al**[7] **and Diana F Gabinsky et. al.**[3].

Intramuscular Diclofenac (75 mg) was be given as rescue analgesic.The mean number of doses required in 24 hours was 3.51, 2.39, 2.54 and 1.76. however statistically insignificant(p>0.05), lesser dose was required in neostigmine and fentanyl combination group. The neostigmine and fentanyl combination decrease the demand of rescue analgesia . Our result coincide with **Lauretti et al**[2]**.**

CONCLUSION

The combination of intrathecal neostigmine and fentanyl with bupivacaine significantly prolonged post operative analgesia as compared to control group as well as bupivacaine and fentanyl or neostigmine groups. However no significantdifference was seen in the onset and duration of motor block in all four groups.

REFERENCES

1. Zhuo M, Gebhast GF.Tonic cholinergic inhibition of spinal mechanical transmission.Pain1991:46:211-222 (S)
2. Lauretti GR et al: Combined Intrathecal Fentanyl and Neostigmine: Therapy for PostoperativeAbdominal Hysterectomy Pain Relief Journal of Clinical Anesthesia 10:291–296, 1998
3. Diana Fernandez-Galinski, Montserrat Rue, Victoria Moral, Carmen Castells, Margarita M. Puig : Spinal anesthesia with Bupivacaine and Fentanyl in geriatric patients. Anesthesia Analgesia 1996; 83 : 537-41.
4. B. N. Biswas, A. Rudra, B. K. Bose, S Nath, S. Chakrabarty, S. B hattacharjee; I ntrathecal Fentanyl with hyperbaric Bupivacaine improves analgesia during Caesarean delivery and in early posto perative period. Indian Journal of Anaesthesiology. 2002 ; 46(6): 469-72.
5. Fareed ahmed,Ashish,AP Verma ,Mamta khandelwal: transdermal nitroglycerine enhances post operative analgesia of intrathaecal fentanyl following abdominal hysterectomies. Australian society of anaesthetists march 2010 vol 38 :285-290
6. Shobhana Gupta (2010) : Post operative Analgesia With Intrathecal neostigmine ;Two different Doses of Neostigmine 75µgms and 50µgms with Heavy Bupivacaine. The internet Journal of Anaesthesiology. 2010 Volume 25 Number1
7. Harbhej Singh, Jay Yang, et al. Intrathecal fentanyl prolongs sensory bupivacaine spinal block. Can J Anaesth 1995, 42(11): 987-91.
8. Uma Srivastava, Aditya Kumar, N.K.Gandhi, Surekha Saxena, Devesh Dutta, Parul Chandra, Saroj Singh: Hyperbaric or plain Bupivacaine combined with Fentanyl for spinal anaesthesia during Caesarean delivery. Indian Journal of Anaesthesia2004;48(1):44-46