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EFFECT OF NEOSTIGMINE AS AN ADJUVANT TO HYPERBARIC BUPIVACAINE (0.5%) IN SUBARACHNOID BLOCK IN LOWER EXTREMITY SURGERIES

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ABSTRACT

Spinal Anaesthesia is commonly used for lower extremity surgery. Hyperbaric Bupivacaine is often used for this purpose. Addition of adjuvants increase duration of Bupivacaine action. Study of the effect of Neostigmine as adjuvant to injection Bupivacaine heavy (0.5%) for spinal anaesthesia. Thirty two (32) ASA grade I & II patients aged 20-60 year were studied, they received 0.5% Bupivacaine (H) with 25-mcg Neostigmine, hemodynamic, reduction in post-operative pain up to 24 hours post operatively was assessed by visual analogue score (VAS) & side effects were studied. Over all 24-hour visual analogue score in-these patient was significantly lower ($p<0.01$). Neostigmine as an adjuvant had no effect on characteristic of spinal anaesthesia ($p>0.05$). First dose of rescue analgesia or duration of complete analgesia was longer. Incidence of bradycardia in these patients was lower($p<0.01$). Incidence of nausea and vomiting was not increased. Neostigmine prolong the duration of spinal anaesthesia. Neostigmine increases the analgesic efficacy when used as adjuvant with 0.5% bupivacaine heavy.

KEYWORDS: Neostigmine, Intrathecal, Bupivacaine, Sub arachnoid block, Lower extremity surgery.

INTRODUCTION

August bier performed the first spinal anesthesia using cocaine in 1889 (1). Presently, spinal anesthesia is a safe, convenient & economical form of regional anesthesia technique (2) & has gained widespread popularity in developing world (3).

Bupivacaine 0.5% (H) was only drug for spinal anesthesia after discontinuation of lidocaine intrathecal drug use. Bradycardia and hypotension are hemodynamic side effects of use of high dose of local anesthetic agent to prolong the duration of analgesia (4).

Various adjuvant like ketamine, clonidine, adrenaline, midazolam, epinephrine, neostigmine and opioids (morphine & fentanyl) have been used with intrathecal bupivacaine (5-10).

Neostigmine is a cholinesterase inhibitor which leads to an increase of the acetylcholine concentration. It has been frequently added to local anesthetics for caudal epidural analgesia (11-12). As an adjuvant neostigmine can effectively prolong the duration of subarachnoid block and could provide better hemodynamic stability during spinal anesthesia (13-17).

In this study we plan to evaluate efficacy & tolerability of intrathecal Neostigmine as adjuvant to hyperbaric bupivacaine in patient posted for lower extremity surgery.

AIM

To study effect of Neostigmine as adjuvant to Hyperbaric Bupivacaine (0.5%) in spinal anesthesia for lower extremity surgery.

OBJECTIVES

- To evaluate the onset & duration of sensory & motor block.
- To evaluate hemodynamics variables (heart rate, blood pressure and oxygen saturation)
- To evaluate the time of use of first rescue analgesia.
- To identify and note the side effects and complications, if any due to addition of Neostigmine as an adjuvant.

MATERIAL AND METHODS

After obtaining the institutional ethical committee clearance & written and informed consent, 32 patient of age 20-60 years of American society of anesthesiologist (ASA) grade I & II, undergoing lower extremity surgery under subarachnoid block were included in the study. Patient were randomly allocated into a group of 32 patient. The sampling frame of study was bound by following Inclusion and Exclusion criteria.

INCLUSION CRITERIA	EXCLUSION CRITERIA
ASA GRADE I & II	Refusal of patient for enrolment under study
Age group 20-60 Years	Patient with history of respiratory, cardiac or hepatorenal disorder.
	Patient allergic to drugs or having severe neurological deficit.
	Patient on medication of adrenoreceptor agonist, digoxin, anticonvulsant or psychotropic substance and allergy to study drugs.
	Patient with bradycardia, hypertension.
	Clotting and bleeding disorder.

The patients were randomly allocated into group of 32 patient each with help of computer generated randomization as under:

32 patient received Injection Neostigmine (25 mcg) with Hyperbaric bupivacaine (0.5%) in spinal anesthesia.

Intravenous (IV) preloading was done with Ringer's lactate as a bolus of 6–8 ml/kg given over 15 min before spinal anesthesia. Patients were premedicated with 0.004 mg/kg injection glycopyrrolate and injection ondansetron 0.1 mg/kg before induction.

A 25-G spinal needle was introduced through the L3–L4 interspace with patient in the sitting position. A total volume of 3.5 ml was injected intrathecally (IT) ,,at a rate of 0.25ml/sec. The intrathecal drug injected was 15 mg hyperbaric bupivacaine (3 ml) plus the test drug (Neostigmine 2 unit in insulin syringe and diluted up to 0.5 ml).

Patients were placed in the supine position immediately after spinal injection. One anesthesiologist prepared the drug and administered the intrathecal drug, while another anesthesiologist, who was blinded to the drug randomization, monitored the intraoperative and post-operative period.

Intraoperative sensory and Motor blockade of lower extremities was for the first 10 min after injection of the intrathecal drug. Blood pressure, heart rate and SpO2 were monitored continuously throughout the surgery.

A decrease in mean arterial pressure of greater than 25% below the baseline preanesthetic value or less than 60 mmHg was treated by incremental doses of 6 mg injection. mephenteramine intravenous. A decrease in heart rate of more than 15% below the baseline or 50 beats per min was treated by injection atropine 0.6mg IV.

Duration of rescue analgesia was the time until visual analogue score (VAS) pain scores were ≥ 4 cm or when the patient's first requested for supplemental analgesia, whichever appeared first. Subsequently, injection diclofenac sodium AQ was administered 1.5mg/kg as the rescue analgesic.

The total number of rescue analgesics administered in 24 hours was noted. Postoperative assessment included pain scores and postoperative nausea and vomiting (PONV) scores (5-point scale) recorded for 24 hour postoperatively. One or more emetic episodes were treated using ondansetron 4mg intravenous. For patients experiencing more than one episode of nausea, the scores were averaged.

RESULTS

32 patients received Injection Neostigmine (25 mcg) in combination with Hyperbaric Bupivacaine (0.5%) in spinal anaesthesia.

Mean age of cases of this Group (37.34 ± 13.97 years). F-1.181, (Pvalue0.312).

In this Group majority of the patients were female 62.5%.

Mean body weight was 57.14 kg (Pvalue 0.467).

Average duration of surgery of This Group 113.53 ± 11.14.

ASA Grade	Group II (n=32)	
	No.	%
Grade I	17	53.1
Grade II	15	46.9
Pvalue-0.747		

Table 1: ASA Grade

Oxygen saturation level was maintained >95% (97-100%) in all the patients during the period of observations.

Average time to achieve peak sensory block (T6) was (6.38±1.07 min)-NOT SIGNIFICANT

Average time to achieve peak motor block (B/S-3) for patients of this Group (6.69±0.97 min)- NOT SIGNIFICANT

Bradycardia	4	12.5%
Nil	28	87.5%
P<0.001%		

Table 2: Incidence of Bradycardia was Significantly Lower in These Patient

Rescue Doses	**PATIENT n=32**	
	No.	**%**
None	2	6.3
One	29	90.6
Two	1	3.1
P<0.001%		

Table 3: Comparison of Number of Rescue Analgesia

Time of requirement of first dose of rescue dose was 149.17 ± 22.58 minutes (P- 0.567)

No. of patients	**Max.**	**Min.**	**Mean**	**S.D.**
32	120.00	440.00	319.25	81.14

Table 4: Duration of Effective Analgesia

Duration of effective analgesia was (319.25± 81.14 min) P<0.001

	Score 2		**Score 3**		**Score 4**		**Score 5**		**Score 6**	
	No.	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**	**No.**	**%**
Patient-32	11	34.4	17	53.1	4	12.5	0	0.0	0	0.0

Table 5: Intergroup Comparison of VAS Score at first rescue dose

VAS score of the patient was significantly lower p < 0.001.

DISCUSSION

Since the first use of spinal anesthesia in the late 19th century, it has emerged as a safer, more economical and highly convenient method of anesthesia as compared to other regional counterpart.

Bupivacaine 0.5% has emerged with a monopoly in the field of drugs used for spinal anesthesia, since the discontinuation of lidocaine intrathecally.

Variation to Bupivacaine are available in form of Hyperbaric Bupivacaine formulated by adding adjuvant to hyperbaric Bupivacaine such as Neostigmine.

Present study was conducted with an aim to study effect of neostigmine as an adjuvant to Hyperbaric Bupivacaine (0.5%) in spinal anesthesia for lower extremity surgery.

Onset and duration of sensory and motor blockade, hemodynamics variables, time of use of first rescue analgesia, side effects and complications of Neostigmine as adjuvant to Hyperbaric Bupivacaine were evaluated.

The inhibition of spinal cholinesterase by Neostigmine results in an increase of endogenous acetylcholine, which is most likely released from intrinsic cholinergic neurons with in the dorsal horn of the spinal cord. These cholinergic neurons terminate in the vicinity of primary afferent express muscarinic receptors.

The endogenous acetylcholine produces analgesic effect through muscarinic presynaptic inhibition of glutamatergic afferents, similar to how it has been described in the neostriatum. Muscarinic receptor antagonists have been shown to reverse the analgesic effects of IT neostigmine. Atonic cholinergic activity is an important prerequisite for the effectiveness of neostigmine.

The enhanced analgesic efficacy of IT Neostigmine results from greater release of spinal acetylcholine from the more intense and prolonged discomfort of postoperative pain, and consequent action at muscarinic M1 and M3 and presynaptic nicotinic receptors present in the cholinergic interneurons at the lamina III and V of the dorsal horn. An action at nicotinic receptors at the dorsal horn ganglion and at the spinal meninges has also been suggested.

Neostigmine increase the time of first rescue analgesia as supported by Lauretti *et al* (18) and Shakya *et al*(19) in their study. Incidence of hypotension and bradycardia was less with neostigmine then Fentanyl and patients were more hemodynamically stable as reported by Carp *et al* (20), Pan and Mok (21) and Shakya *et al* (19) in their study.

Time to reach maximal level of sensory block, peak level and development of complete motor block was not influenced by use of intrathecal Neostigmine, as demonstrated by Lauretti *et al* (18) in patient undergoing vaginal hysterectomy and Almeida *et al*(22).

CONCLUSION

From the above results and study conducted, we conclude that Neostigmine as an adjuvant prolong the duration of spinal anesthesia. Neostigmine increases the analgesic efficacy when used as an adjuvant with Hyperbaric Bupivacaine (0.5%) in lower extremity surgery.

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