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NEOSTIGMINE;
AS AN ADJUNCT TO INTRAVENOUS REGIONAL ANESTHESIA

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ABSTRACT… Objectives: To compare the effect of Neostigmine as an Adjunct to 0.5% Lignocaine for increasing the duration of anesthesia and analgesia. **Study Design:** Randomized controlled trial. **Setting:** Department of Anesthesiology, Nishtar Hospital, Multan. **Period:** January 20014 to January 2015. **Material and Methods:** One hundred (100) patients were selected for this study. Microsoft Excel 2013 was used for data analysis. Frequacy and percentage were used to present categorical varibales and mean±standard deviation for numerical variables. **Results:** There was a rapid onset of Sensory and motor blocks in neostigmine group, 3.9±2.5 minutes for sensory block and 5.8±2.3 minutes for motor block versus 9.3±2.2 minutes and 13.3±2.0 minutes respectively in control group. The time of recovery of sensory and motor blocks was delayed in neostigmine group as compared to the control group patients. The surgeons agreed that the anesthesia was perfect in 46 (92.0%) cases in neostigmine group and in control group IVRA declared to be perfect in only 34 (68.0%) cases. Dryness of operative field was same between the two groups. **Conclusion:** The addition of neostigmine in lignocaine solution for intravenous regional anesthesia improves the quality of anesthesia and analgesia.

Key words: Lignocaine, Neostigmine, Intravenous regional anesthesia.

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INTRODUCTION

The immediate and most anxious problem in patients undergoing any surgical intervention is pain. Post-operative pain can make the patient very restless. Painful stimulus produced by a surgical incision results in hyper excitable state leading to post-operative pain.[1,2] Nowadays, as the life gets busier, the scope and necessity of Day Care Surgery are also amplifying. Day care surgical units provide services to the patients with hospital stay less than one day.[3] For short operations involving upper limbs, Intravenous regional anesthesia is considered to be a reliable anesthesia technique.[4,5] Pain resulting from tourniquet inflation and inability to provide post-operative analgesia are the main limitations of IVRA.[6] But it requires lesser analgesia and antiemetics during recovery and hence more favorable patient outcomes. It also requires less nursing care in post anesthesia care unit and promotes expedited hospital discharge.[7]

An ideal IVRA solution should have the rapid onset, reduced dose of local anesthetic and prolonged analgesia. This is attained by addition of various adjuncts to local anesthetics like morphine, fentanyl, clonidine, tramadol and non-steroidal anti-inflammatory drugs like ketorolac.[8,9] Intrathecal administration of neostigmine (antidote of muscle relaxants) provides analgesia by inhibiting the effect of spinal card acetylcholine receptors.[10,11] Therefore neostigmine as an Adjunct to 0.5% Lignocaine can increase the duration of anesthesia and decrease the degree of post-operative pain. This study was conducted to evaluate the quality of anesthesia and analgesia when neostigmine is used as an adjunct to 0.5% Lignocaine in intravenous regional anesthesia in patients undergoing hand and arm surgery.

MATERIAL AND METHODS

This trial was carried out in the department of anesthesiology, Nishtar Hospital, Multan from January 2014 to January 2015, after obtaining

permission from the ethical committee of the institution. A total of 100 patients (two groups of 50 patients in each group) were selected for this study, who were undergoing upper limb surgery having age 20 to 50 years. Informed consent was taken from all patients and randomization was done. Group A (Control Group): received Inj. Lignocaine 0.5% only in IVRA whereas; Group B (Neostigmine Group) received Inj. Lignocaine 0.5% + Inj. Neostigmine 0.5 mg.

Microsoft Excel 2013 was used for data analysis. Frequency and percentages were used to present categorical variables and mean±standard deviation for numerical variables.

RESULTS

In this study, One hundred patients were included. There was no statistically significant difference in demographic variables of the patients and ASA status. There was a rapid onset of Sensory and motor blocks in neostigmine group, 3.9±2.5 minutes for sensory block and 5.8±2.3 minutes for motor block versus 9.3±2.2 minutes and 13.3±2.0 minutes respectively in control group. The time of recovery of sensory and motor blocks was delayed in neostigmine group as compared to the control group patients.

Before tourniquet application, there was no significant difference between the heart rate, mean arterial pressures, and oxygen saturation in control and neostigmine group. Heart rate reduced slightly after inflation of tourniquet and induction of anesthesia in neostigmine group. There was no dissimilarity between the mean arterial pressures and oxygen saturation between the two groups. Perfect anesthesia (declared by surgeons) was more in neostigmine group. The surgeons agreed that the anesthesia was perfect in 46 (92.0%) cases in neostigmine group and in control group IVRA declared to be perfect in only 34 (68.0%) cases. Dryness of operative field was same between the two groups.

	Group-A (50)	Group-B (50)
Age (years)	29.3±11.5	30.7±10.7
Weight (Kg)	58.6±7.12	57.9±6.23
Male	34 (68%)	34 (68%)
Female	12 (24.0%)	11 (22.0%)
ASA Status of Patients		
ASA-I	36 (72.0%)	14 (28.0%)
ASA-II	38 (76.0%)	12 (24.0%)

Table-I. Demographic data and ASA status of Patients
Values are mean ± SD or number and percentages

DISCUSSION

Intravenous regional anesthesia (IVRA) is achieved by administration of local anesthetic agents in the peripheral blood vessels. IVRA is a routinely used method in the isolated arm and forearm surgeries. For times, there was a quest for finding a local anesthetic along with an adjuvant drug e.g. opioids, muscle relaxants and NSAIDS that would allow prolonged duration of anesthesia and analgesia.

Acetylcholine receptors are also present in peripheral nerves; peripheral cholinergic antinociception is initiated by neuronal hyperpolarization and nitric oxide pathways.[12,13] Spinal endogenous Ach receptors plays a significant role in mediating the analgesic effect both by muscarinic and nicotinic receptors that are present in the peripheral tissues.[14] Some studies have confirmed peripheral analgesic effect of neostigmine on inflamed isolated joints in rats and animals.[15,16] However, Van Elstraete et al. showed that neostigmine failed to achieve its analgesic action in axillary nerve blocks in patients undergoing carpal tunnel release surgery.[17]

		Control Group (n=50)	Neostigmine Group (n=50)
Sensory Block (min)	Onset time	9.3 ±2.2	3.9 ±2.5
	Recovery time	3.1±1.9	7.8 ± 1.7
Motor Block (min)	Onset time	13.3±2.0	5.8±2.3
	Recovery time	2.3±0.8	5.6±1.5

Table-II. Onset and Recovery of Sensory and Motor Blocks (min)

Variable		Group A (n=30)	Group B (n=30)
Heart Rate (Beats/min)			
Before tourniquet		78.8 ± 5.6	77.7 ± 4.9
Immediately after tourniquet application		82.6±6.2	80.7 ± 10.5
After 20.min.		84.4 ± 8.3	69.7 ± 9.7
After tourniquet release		80.8 ± 6.6	72.3 ±9.3
Mean Arterial Pressures (mmHg)			
Before tourniquet		98.7 ± 12.9	97.9 ± 7.3
Immediately after tourniquet application		97.3 ±11.2	96.8 ± 7.2
After 20.min.		94.9 ± 11.2	93.8 ± 6.9
After tourniquet release		92.5 ± 5.3	90.1 ± 4.1
SpO^2			
Before tourniquet		98.1±0.5	98.6 ±0.4
Immediately after tourniquet application		98.9±0.8	98.2 ± 0.5
After 20.min.		98.7 ± 0.8	99.0 ± 0.2
After tourniquet release		98.8 ±0.8	98.4 ± 0.9
Surgeons Satisfaction rate			
Quality of Anesthesia	Perfect	34 (68.0)	46 (92.0)
	Acceptable	16 (32.0)	4 (8.0)
Dryness of operative field	Perfect	49 (98.0)	49 (98.0)
	Acceptable	1 (2.0)	1 (2.0)

Table-III. Heart rate, Mean Arterial Pressures and SpO_2 Comparison.

The reason for the absence of analgesic action of neostigmine may be due to the lack of inflammatory process and dense lipid coverings of nerves.[17,18] Bouaziz et al. showed that neostigmine failed to achieve analgesic effects in a carrageenan-induced hyperalgesia rat model with inflamed tissues.[19] Neostigmine used in this study have a very different mechanism of action. In IVRA, anesthetic agents are injected very close to the surgical site, and the tourniquet-induced ischemia exerts nerve penetration by oxidative stress and disturbing the blood-nerve barrier.[20] ACh receptors are responsible for the action of neostigmine in peripheral analgesia.[21] neostigmine improve muscle relaxation thereby improve overall analgesia and facilitate in fracture reduction.[22]

In this study, bradycardia was the most common side effect the reason for this may be the systemic absorption of neostigmine. However, tourniquet release did not further decreases the heart rate. Nausea occured in one patient perhaps due to systemic absorption of IVRA.

CONCLUSION

The addition of neostigmine in lignocaine solution for intravenous regional anesthesia improves the quality of anesthesia and analgesia.

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AUTHORSHIP AND CONTRIBUTION DECLARATION

Sr. #	Author-s Full Name	Contribution to the paper	Author=s Signature
1	Dr. Aamir Furqan	Conceived, Designed and did statistical analysis.	
2	Dr. Adnan Aslam	Manuscript writing and data analysis.	
3	Dr. Afifa Zahoor	Data Collection and help in manuscript writing.	