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Neostigmine as an Adjunct to 0.5% Lignocaine Quality of Anaesthetia and Analgesia in Intravention Regional Anaesthesia

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ABSTRACT
Objective:- To **c**ompare the duration of anaesthesia and the degree of post operative pain relief. **Material and methods**:- This Interventional type of study was carried out in the Anaesthesia department, Nishtar Hospital Multan from January 2017 to January 2018. A total of 100 patients (two groups of 50 patients in each group). **Results:-** The onset of anaesthesia and quality of anaesthesia were better in neostigmine group ($P<0.05$). Post operative pain relief was also better. No significant difference in hemodynamics and no adverse effects were observed. **Conclusion:-** With the addition of neostigmine in traditional lignocaine solution for IVRA the quality of anaesthesia and analgesia is improved.
Key words:- Intravenous regional anaesthesia, IVRA, lignocaine, neostigmine.

INTRODUCTION

The immediate and most concerned problem of a patient undergoing any surgical procedure is pain. Anticipation for post operative pain makes the patient too much anxious. The International Association for the Study of Pain defines Pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage[1,2]. So it can be understood that there is interplay between the objective, physiologic sensory aspects of pain and its subjective, emotional and psychological components.
While dealing with pain, a clinician must have a thorough knowledge of anatomical pathways concerned with the transmission of pain and physiology of perception and transmission of pain. Painful stimulus like that produced by a surgical incision can lead to a hyper excitable state which is the major cause of post operative pain. Now a day, as the life is getting busier and busier, the scope and necessity of Day Care Surgery is also augmenting. Day care surgical units provide services to the patient whose hospital stay is expected to be less than 24 hours and then the patient can be discharged[3]. In these units, intravenous regional anaesthesia is one of the safest and most reliable forms of anaesthesia for short surgical procedures on the upper extremity[4,5]. However its use has been limited by tourniquet pain and inability to provide post operative analgesia[6]. But on the other hand, it has been associated with a more favorable patient recovery than general anaesthesia and patient also require lesser analgesia and anti emetics during recovery as compared with general anaesthesia. It also requires less nursing care in post anaesthesia care unit and promotes expedited discharge from the hospital[7].
An ideal intra venous regional anaesthesia solution should have rapid onset, reduced dose of local anaesthetic and prolonged analgesia. At present, this may only be achieved by addition of various adjuncts to local anaesthetics like morphine, fentanyl, clonidine[8], tramadol and non steroidal anti inflammatory drugs like ketorolac[9]. Neostigmine is a drug that has been used to reverse the effects of muscle relaxants[10]. Intrathecal administration of neostigmine has proved to cause analgesia by inhibition of acetylcholine receptors in the spinal cord[11]. There are also acetylcholine receptors in peripheral nerves. Therefore, this study is designed to evaluate the effects of neostigmine when added to 0.5% Lignocaine in intravenous regional anaesthesia.

MATERIAL AND METHODS;

This Interventional type of study was carried out in the Anaesthesia department, Nishtar Hospital Multan from January 2017 to January 2018. A total of 100 patients (two groups of 50 patients in each group).

RESULTS

In this study I compared the quality of anesthesia and post operative analgesia in patients undergoing hand and arm surgery divided into two groups of traditional IVRA solution of 40ml of 0.5% lidonaciane in group A and addition of neostigmine 0.5mg in traditional IVRA solution in group B. Hundred patients, fifty patients in each group were included in the study. There were no statistically significant difference in demographic data including age, weight and gender of the patients and ASA status in both groups. (Table-1) Sensory and motor block onset times were statistically shorter in the neostigmine group ($P < 0.05$). Sensory and motor block recovery times were statistically prolonged in this group also ($P < 0.05$) (Table 3). There was no statistical difference between groups when compared for heart rate before and after tourniquet inflation, after anesthetic injection, and at 1 and 5 min, but at 10, 15, 20, and 40 min, there was a statistically significant decrease in the neostigmine group when compared with the control group ($P < 0.05$) (Table 4). There was also no statistical difference between groups when compared for MAP and SpO2 at any time (Table 5 and 6). Anesthesia quality determined by the surgeon and dryness of the operative field were found statistically better in the neostigmine group ($P < 0.05$) (Table 7).

Table 1: Comparison of demographic data

	Group-A (50)	Group-B (50)
Age (years)	27.8 + 10.3	26.7 + 9.1
Weight (Kg)	62 + 7	63 + 6
Male	34 (68%)	34 (68%)
Female	16 (32%)	16 (32%)

Values are mean ± SD or number and %ages

Group A: Inj. Lignocaine 0.5%

Group B: Inj. Lignocaine 0.5% + Inj. Neostigmine 0.5 mg

Table 2: Comparison of ASA status

	Group-A (50)	Group-B (50)
ASA-I	34 (68%)	16 (32%)
ASA-II	35 (70%)	15 (30%)

Table 3: Comparison of Onset and Recovery Times of Sensory and Motor Block (min)

	Group A (n=30)	Group B (n=30)
Sensory block onset time	10 + 2	4 + 2
Sensory block recovery time	3 + 1	7 + 2
Motor block onset time	14 + 1	6 + 2
Motor block recovery time	2 +1	5 + 2

P-value < 0.05

Table 4: Comparison of Heart rate

	Group A (n=30)	Group B (n=30)
Before tourniquet	75.4 ± 4.4	74.5 ± 9.4
At tourniquet	79.6 ± 6.3	80.2 ± 13.5
After 1.min.	80.7 ± 5.6	79.7 ± 14.4
After 5.min.	78.5 ± 6.6	76.5 ± 14.8
After 10.min.	78.7 ± 7.9	71.2 ± 14.3*
After 15.min.	78 ± 7.6	70.6 ± 13.9*
After 20.min.	82.4 ± 6.9	68.4 ± 14.5*
After 40.min.	80.5 ± 7.6	68.5 ± 7.6*
After tourniquet release	79.7 ± 5.6	74.2 ± 8.2

P-value < 0.05

Table 5: Comparison of Mean arterial pressure

	Group A (n=30)	Group B (n=30)
Before tourniquet	94.4 ± 13.6	91.2 ± 8.10
At tourniquet	98.5 ± 13.9	95 ± 5.9
After 1.min.	96.6 ± 14.2	93.8 ± 6.60
After 5.min.	97.8 ± 13.5	95.4 ± 7.1
After 10.min.	95.2 ± 15.2	93.1 ± 7.5
After 15.min.	96.7 ± 12.6	94.2 ± 8.4
After 20.min.	93.6 ± 12.6	92.3 ± 7.3
After 40.min.	94.6 ± 12.3	92.2 ± 6.4
After tourniquet release	93.4 ± 6.4	90.4 ± 6.7

Table 6: Comparison of SpO_2

	Group A (n=30)	Group B (n=30)
Before tourniquet	98.8 ± 0.6	98.9 ± 0.5
At tourniquet	98.8 ± 0.7	98.8 ± 0.6
After 1.min.	98.8 ± 0.7	98.9 ± 0.7
After 5.min.	98.8 ± 0.7	98.8 ± 0.7
After 10.min.	98.9 ± 0.4	98.8 ± 0.6
After 15.min.	98.8 ± 0.7	98.9 ± 0.5
After 20.min.	98.9 ± 0.8	98.9 ± 0.7
After 40.min.	98.8 ± 0.7	98.8 ± 0.7
After tourniquet release	98.7 ± 0.7	98.9 ± 0.7

Table 7: Quality of Anesthesia assessed by a Surgeon, and Dryness of the Operation Field

	Group A (n=30)	Group B (n=30)
Quality of anesthesia (surgeon)	Acceptable	Perfect
Dryness of the operation field	Perfect	Perfect

DISCUSSION

IVRA is a technique in which anaesthesia is achieved by instillation of local anaesthetic in a limb through peripheral blood vessels and produces its effects by absorption of local anesthetic. This technique is widely used in isolated forearm and hand surgery. For times, there was a quest for finding a local anesthetic with addition of an adjuvant drug which would allow prolonged duration of anaesthesia and post operative analgesia. For this, various drugs like tramadol, opiods, muscle relaxants and NSAIDs have been frequently used. Studies have shown that there are ACh receptors in peripheral nerves, and in vitro studies have shown that peripheral cholinergic antinociception is caused by neuronal hyperpolarization and by modulation of nitric oxide pathways. ACh induces analgesia via increasing cyclic GMP by generation of nitric oxide[12,13]. Spinal endogenous ACh plays an important role in mediating the analgesic effect of systemic morphine through both muscarinic and nicotinic receptors that are also present in the peripheral tissue[14]. The peripheral analgesic effect of neostigmine has been demonstrated in an animal model of inflamed knee joint in rats[15]. Another study of intraarticular administration revealed peripheral analgesic effects in humans[16]. However, a recent study performed by Van Elstraete et al in patients undergoing carpal tunnel release showed that neostigmine added to lidocaine for axillary plexus block lacked an analgesic action[17]. Peripheral inflammatory conditions, when present, enhance analgesic actions of locally administered opioids and cholinergic drugs[17,18]. The reason for neostigmine's lack of analgesic action may be the lack of an inflammatory process and intact dense lipid coverings of nerves [63]. Yet, controversy persists. In a study performed by Bouaziz et al neostigmine lacked analgesic effects in a carrageenan-induced hyperalgesia rat model with inflamed tissue[19].

Therefore, we used neostigmine in a block with a very different mechanism of action. IVRA local anesthetic and adjuvants are injected very near to the surgical site, and the tourniquet causes ischemia, which distorts nerve

penetration by oxidative stress and affects the blood-nerve barrier[20]. Existing ACh receptors in peripheral nerves are also responsible for the action of neostigmine in peripheral analgesia, and ACh plays a role in newly discovered sensory regulatory mechanisms controlled by the motor system[21]. Study results indicate that ACh receptors are present in the soma of many petrosal ganglion neurons, thus supporting the idea that under normal conditions, peripheral sensory processes may be associated with Ach[22]. The most frequent side effect seen in our study was bradycardia, which may have been because of systemic absorption of neostigmine or its escape during tourniquet inflation. Tourniquet release did not further decrease HR. Nausea seen in one patient may also have been due to systemic absorption. Results of a systematic review by Choyce and Peng [69] suggested that nonsteroidal antiinflammatory drugs (NSAIDs) have the most to offer as adjuncts to IVRA when compared with others. NSAIDs, either as part of IVRA or wound infiltration, resulted in an analgesic benefit lasting longer than the same dose parenterally administrated. Our results revealed a clinically minor postoperative analgesia effect when compared with NSAIDs. Muscle relaxants improve muscle relaxation, facilitate fracture reduction, and improve overall analgesia[23]. However, there is a risk of residual muscle weakness that can last several hours. Neostigmine improved muscle relaxation with residual weakness lasting for only a few minutes. Our study presents information about the clinical use of neostigmine as an adjunct in IVRA, however it may also be a useful model for studying the peripheral action of neostigmine in the absence of central effects.

CONCLUSION

With the addition of neostigmine in traditional Lignocaine solution for IVRA the quality of anaesthesia and analgesia is improved.

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