USE OF NEOSTIGMINE TO AUGMENT INTRAVENOUS REGIONAL ANESTHESIA USING LIGNOCAINE IN UPPER LIMB SURGERY

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ABSTRACT

Objectives To evaluate the effects of neostigmine on onset and duration of Intravenous regional anesthesia (IVRA) when added to lignocaine.

Study Design: Randomized control trial.

Place and duration of study: Combined Military Hospital Rawalpindi from 21 September 2006 to 23 April 2008.

Patients and Methods: One hundred patients undergoing hand surgery were randomly assigned to two groups to receive IVRA. The control group received 1mililiter (mL) of saline plus 3 miligram per kilogram(mg/kg) of lignocaine diluted with saline to a total dose of 40 mL, the study group received 0.5 mg (1ml) of neostigmine plus 3 mg/kg of lignocaine diluted with saline to a total dose of 40 mL. Sensory block and motor block onset and recovery were noted. Heart rate, mean arterial blood pressure, and oxygen saturation values were noted before surgery 1min, 5 min, 10 min, 20 min, and 40 min and after tourniquet release. Time to first analgesic requirement was also noted.

Results: The mean sensory block onset was 4.14 min as compared to 10.1 min in control group. Mean value of motor block onset was 6.3 min as compared to 13.8 min in control group.similarly mean for sensory recovery was 6.9 min as compared to 3.1 min for control group. Mean value for motor recovery was 5.17 min as compared to 2.17 min in control group.

Experiment group had their demand for analgesics after a mean of 35.3 min and control group had their analgesia after 16.5 min. There was highly significant difference in all the variables.

Conclusion: We concluded that neostigmine as an adjunct to lignocaine improves quality of anesthesia and is beneficial in IVRA.

Keywords: Intravenous regional anesthesia, Lignocaine, Neostigmine.

INTRODUCTION

In 1908 Karl August Bier, Professor of Surgery in Berlin, described a new method of producing analgesia of a limb which he named 'vein anesthesia'[1]. IVRA is a safe and effective regional anesthetic technique but is limited by rapid offset of analgesia. Many agents have been added to improve analgesia, but only Nonsteroidal anti-inflammatory drugs have shown benefits[2,3]. It has been limited by tourniquet pain, inability to provide postoperative analgesia, and lack of a bloodless field for microsurgical repairs[4].

A recent study that added neostigmine 500 µg or placebo to prilocaine 3 mg/kg in IVRA showed reduction in sensory and motor block onset time and prolongation of time to first analgesic request in the neostigmine group[5].

The IVRA is easy to perform, with rapid onset of analgesia and safe to practice, when proper patient monitoring is established and a local anesthetic solution with low systemic toxicity is used. When choosing this technique of regional anesthesia it is an important condition that the operative procedure has to be finished before the tourniquet of the upper arm is released. Immediately after this cuff-release and recirculation of the arm analgesia will diminish. When using prilocaine or mepivacaine as local anesthetic drug a complete surgical analgesia of 30 to 45 min can be achieved. Long-acting local anesthetics should not be used because of their increased systemic toxicity under the aspect of drug wash-out at the end of the procedure or in terms of inadvertent cuff release[6].

The ideal intravenous regional anesthetic solution should offer rapid onset, reduced dose, reduced tourniquet pain and prolonged post

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deflation analgesia. At present this is achieved by various adjuncts to local anesthetics that is morphine, pethidine, fentanyl, sufentanil and clonidine.[7] This study was designed to evaluate the effect of neostigmine when added to lignocaine in IVRA.

PATIENTS AND METHODS

This randomized controlled trial (RCT's) was conducted in the department of Anesthesiology Combined Military Hospital Rawalpindi, after approval of hospital ethics committee and informed written consent from the patients from 21 September 2006 to 23 April 2008.

A total of one hundred patients, ASA physical status I or II, scheduled for upper limb and hand surgery were included in our study. Sampling was non-probability convenient. The cases were randomized to two groups, A and B, each comprising fifty patients. Group A was control group and group B was the neostigmine group. All patients were premedicated with 0.01mg per kg body weight, midazolam.Two cannulae were passed, one on the dorsum of the hand of operating arm to inject the drug combination and other on the opposite arm for crystalloid infusions. The operating arm was elevated for two minutes and then exanguinated. Double pneumatic tourniquet were placed arouned the upper arm and the proximal cuff was inflated to 250 mm of Hg. Circulatory isolation of the arm was confirmed by absence of peripheral pulses. Group A received 1.0 ml normal saline plus 3 mg/kg lignocaine diluted to a total dose of 40 ml. Group B received 0.5 mg neostigmine in 1 ml plus 3 mg/kg lignocaine diluted to a total dose of 40 ml. An anesthesiology resident blinded to the injection administerad the drug over one minute.

Sensory block was assessed by a pinprick performed by syringe needle, every 30 seconds after giving the drug. Complete motor block was noted, when no voluntary movement of fingers was possible. Mean arterial blood pressure, heart rate and oxygen saturation were monitored. At the end of surgery, the tourniquet deflation was performed (maximum at 2 hours). Sensory recovery time was noted (time elapsed after tourniquet deflation up to recovery of pain in all dermatomes determined by pinprick test). Motor block recovery time was noted (the time elapsed after tourniquet deflation up to movement of fingers). First analgesic requirement time was also noted (the time elapsed after tourniquet release to first patient request of analgesic.

Statistical analyses were performed using SPSS version15. Descriptive statistics were used to describe the date. Independent sample t-test was used to compare study variables between the two groups. P-value<0.05 was considered as significant.

RESULTS

Sample for control group was 50 patients and experiment group was also 50 patients with a male 72% and female 28%. In control group male were 56% and female patients were 44%. Mean age in experiment group was 34.2 years and mean age in control group was 36.3 years. Both the groups were compareable with respect to gender (P>0.05) and age (P>0.05).

There were five variables which we were comparing with the control group and all had significant difference from the control group. The mean sensory block onset was 4.14min (SD=1.02) as compared to 10.1 min (SD=1.64) in control group (*P*<0.001). Mean value of motor block onset was 6.3 min with standard deviation of 0.94 as compared to 13.8min (SD=0.54) in control group (*P*=0.000). Similarly mean for sensory recovery was 6.9min (SD=1.03) as compared to 3.1 min with standard deviation of 0.51 for control group (P<0.001). Mean value for motor recovery was 5.17 min (SD=1.22) as compared to 2.17 min (SD=0.37) in control group (P<0.001).

Experiment group had their demand for analgesics after a mean of 35.3min (SD=4.85) and control group had their analgesia after 16.5 min with standard deviation of 5.50 (P<0.001).

DISSCUSSION

These results are supported by many national and international studies. Turan et al, conducted the study to evaluate the effects of Neostigmine when added to prilocaine for IVRA. It showed neostigmine as an adjunct to prilocaine improves quality of anesthesia and is

beneficial in IVRA.[5] Sensory block onset was 4 min and motor block onset was 6 min similarly in this study sensory recovery was 7 min and motor recovery was 5 min but they used prilocaine instead of lignocaine.

McCartney et al results were very different than our study. This study showed that neostigmine 1 mg when added to lidocaine for IVRA produces no advantage in terms of sensory block or quality and duration of postoperative analgesia[8].

One important thing in their study was that both groups had a significant anesthetic technique failure rate. This raises suspicion that there is something lacking in their method because lignocaine alone should have acted upon if neostigmine did not enhance the effect of lignocaine. The lack of analgesic effect in this study may be because neostigmine is a quaternary amine and may have difficulty crossing the neuronal membrane to have an effect at the proposed site of action on sensory nerves. However, this is unlikely as neostigmine has no difficulty reaching the neuromuscular junction to reverse neuromuscular block.

Study done by Van Elstraete *et al* added Neostigmine to lidocaine in axillary plexus block for postoperative analgesia. They concluded that it does not seem to be of clinical value for peripheral nerve blocks. The reason for neostigmine's lack of analgesic action may be the lack of an inflammatory process and intact dense lipid coverings of nerves[9]. But the peripheral analgesic effect of neostigmine has been demonstrated in an animal model of inflamed knee joint in rats.[10]

Recently, epidural and spinal administration of neostigmine was shown to produce a dose-dependent analgesia. However, this analgesia was limited by adverse effects[11].

In another study they found that the Epidural neostigmine in lidocaine produced a dose-independent analgesic effect (approximately 8 h) compared to the control group (approximately 3.5 h), and a reduction in postoperative rescue analgesic consumption without increasing the incidence of adverse effects.[12]

Inspite of many positive results by many colleagues negative results are also shown by Bouaziz and colleagues in their study concluded that Neostigmine added to Mepivacaine in Axillary plexus block does not prolong postoperative sensory block, but it does cause a relatively high incidence of side effects.[13]

The pharmacological profile of prilocaine and lidocaine are similar and study by McCartney *et al* could not explain why neostigmine has an effect on sensory block onset and time to first analgesic request with prilocaine and not with lidocaine. In a study with prilocaine, the investigators also gave patients the muscarinic antagonist atropine 10μg/kg as premedication, which suggest that any anesthetic or analgesic benefit was as a result of nicotinic agonism.

In our study lignocaine neostigmine produced a decrease in motor block onset time, which could be explained by the nicotinic agonist effect of neostigmine at the neuromuscular junction.

We did not use intravenous neostigmine but in one study intravenous neostigmine enhancea the analgesic effect of epidural anesthesia, mediated by a cholinergic muscarinic mechanism. However, in clinical practice, it does not seem to be useful, because of the side effects[14].

Various other adjuncts are also used by researchers which conclude that adjuncts are always helpful in IVRA. Memis et al, added dexmedetomidine to lidocaine for intravenous regional anesthesia. They concluded that the addition of 0.5 micro g/kg dexmedetomidine to lidocaine for IVRA improved quality of anesthesia and perioperative analgesia without causing side effects[15] .

In a study by Esmaoglu *et al*, addition of dexmedetomidine to local anaesthetic solution in IVRA improved the quality of anaesthesia and decreased analgesic requirements, but had no effect on the sensory and motor blocks onset and regression times[16].

The study by Bigat *et al*, concluded that the addition of 8 mg dexamethasone to lidocaine for IVRA in patients undergoing hand surgery improves postoperative analgesia during the first postoperative day[17].

Another study suggests a questionable benefit for adding 2 mg of morphine sulfate to a Bier block solution.[18]

Acalovschi *et al*, demonstrated that 0.25% tramadol solution containing 100 mg tramadol is not effective as a sole drug, but may improve the action of 0.5% lidocaine for intravenous regional anesthesia. The increased incidence of side effects may limit the clinical use of tramadol[19].

Study by Acalovschi I et al, states that Meperidine has local anesthetic action on the peripheral nerve in vivo, but that its single use for IVRA should be a second choice for patients allergic to local anesthetics[20]. Reuben *et al* showed that Meperidine may be a useful addition to 0.5% lidocaine for intra venous regional anesthesia. 30 mg is the optimal dose of meperidine with respect to postoperative analgesia. However, this dose caused a significant incidence of sedation, dizziness, and postoperative nausea and vomiting[21].

Very recent studies evaluated the analgesic effect of nitroglycerine (NTG) when added to lidocaine in IVRA. Selda *et al*, concluded that the addition of NTG to lidocaine for IVRA improves sensory and motor block, tourniquet pain, and postoperative analgesia without side effects[22].

Sen, *et al* concluded that the addition of lornoxicam to lidocaine for intravenous regional anaesthesia shortens the onset of sensory and motor block, decreases tourniquet pain and improves postoperative analgesia without causing any side effect[25].

CONCLUSION

Neostigmine as an adjunct in IVRA is helpful in reducing sensory motor onset and prolonging recovery as well as post operative analgesic requirement.

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