

Anesthetic and Analgesic Effect of Neostigmine when Added to Lidocaine in Intravenous Regional Anesthesia

Alaa Mohammed Atia* and Khaled Abdel-Baqy Abdel-Rahman

Department of Anesthesia and Intensive Care, Faculty of Medicine, Assiut University, Egypt

*Corresponding author: Alaa M Atia, Department of Anesthesia and Intensive Care, Faculty of Medicine, Assiut University, Egypt, Tel: 0201223591937; E-mail: alaaguhina@yahoo.com

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Abstract

Background: Intravenous regional anesthesia (IVRA) has various advantages during short surgical procedures in upper and lower limbs, but one of its disadvantages is minimal postoperative pain relief.

Aim of the study: To evaluate the anesthetic and analgesic effect of adding 1 mg neostigmine to 0.5% lidocaine in IVRA.

Patients and methods: This randomized double blind controlled clinical trial was carried out at Assiut University Hospital after the approval of its Ethical committee and after obtaining an informed consent from all the patients. Eighty ASA I or II patients who were scheduled for elective hand and forearm surgery were included. We excluded patients with chronic pain syndrome, Reynaud disease, sickle cell anemia, diabetes, pregnancy, lactation, drug allergy and psychological disorders. Patients were randomly assigned to control group who received 3 mg/kg 0.5% lidocaine plus 1 ml normal saline in 40 ml volume and neostigmine group who received 3 mg/kg 0.5% lidocaine plus 1 mg neostigmine in 40 ml volume. Patients were assessed for onset and recovery from the sensory and motor blocks, postoperative pain, analgesic request and incidence of complications. Results No statistically significant differences were observed between groups as regards demographic data, anesthetic or analgesic criteria or the incidence of complications .

Conclusion: Addition of 1 mg neostigmine to 0.5% lidocaine in IVRA has no anesthetic or analgesic effect, and there is no increase in the incidence of complications. There are no biological facts that support its use as adjuvant to local anesthetic agents in IVRA.

Keywords: Neostigmine; Lidocaine; Intravenous regional anesthesia; Analgesic effect; Anesthetic

This study was designed to evaluate the anesthetic and analgesic effects of adding 1 mg neostigmine to 0.5% lidocaine in IVRA.

Introduction

Intravenous regional anesthesia (IVRA) was first introduced by Karl August Bier in 1908 [1]. IVRA is considered as an easy technique with high success rate [2] and low cost suitable for short operative procedures in upper and lower limbs [3].

IVRA has also some disadvantages which include administration of high dose of local anesthetic, poor muscle relaxation, slow onset, tourniquet pain, nerve injuries, compartment syndrome, widespread petechial, skin discoloration and minimal postoperative pain relief [4,5]. Various adjuvant drugs have been evaluated in conjunction with LA to improve IVRA block with variable results [2].

Neostigmine is a typical cholinesterase inhibitor. It increases the level of acetylcholine (ACh) and indirectly stimulates both nicotinic and muscarinic receptors. In anesthesia neostigmine is a drug that has been used for reversal of residual neuromuscular block. Administration of neostigmine by intrathecal and epidural routes has been found to cause analgesia by inhibition of the breakdown of ACh in the spinal cord [6,7]. Some recent studies did not find significant effects in peripheral nerve blocks and IVRA [8,9].

Methods

This randomized double blind controlled clinical trial was carried out at Assiut University Hospital after approval of its Ethical committee and obtaining informed consents from all patients.

We included eighty unselected ASA physical status I or II between 25 and 60 years of age who were scheduled for elective hand and forearm surgery with estimated time of surgery of less than 1 hour. We excluded patients with chronic pain syndrome, Reynaud disease, sickle cell anemia, diabetes, pregnancy, lactation, drug allergy and psychological disorders. Patients were randomly assigned using computer generated random numbers into one of two groups: The control group (group C, n=40) received 3 mg/kg 0.5% lidocaine plus 1 ml normal saline while the neostigmine group (group N, n=40), received 3 mg/kg 0.5% lidocaine plus 1 mg neostigmine. The study drugs were made to volume of 40 ml for both groups to avoid bias.

An intravenous line was placed into the dorsum of the hand to be operated upon for injection of the study drugs. A second IV line was placed into the other upper limb for fluids and emergency drugs administration. Patients were monitored with ECG, pulse oximetry and noninvasive blood pressure. Following exsanguination of the arm

by its elevation for 1-3 minutes and wrapping Esmarch bandage, a pneumatic cuff was applied around the upper third of the arm and inflated to at least 100 mmHg above the patient's systolic pressure and the Esmarch bandage was removed, 40 ml of the study drug was then injected over one minute. When anesthesia was established, a second distal tourniquet was applied and inflated followed by release of the proximal one. At the end of surgery and after at least half an hour of intravenous local anesthetic injection the tourniquet was gradually deflated and all patients were transferred to the post anesthesia care unit. Intraoperative and postoperative bradycardia defined as heart rate <50 beat/min was treated with 0.5 mg intravenous atropine and intra- or postoperative hypotension defined as systolic arterial blood pressure <40% of the baseline was treated with intravenous fluids and/or intravenous 10 mg ephedrine.

Patients assessed their pain using visual analogue scale (on 10 points scale, 0-10) at half an hour interval. Patients whose pain score exceeds 3 were given 30 mg ketorolac and such was repeated on patient request. Intractable pain was managed with pethidine 100 mg IM. The onset of sensory block was assessed every minute with 22 gauge short beveled needle for pinprick and a piece of cotton for touch. The motor function was assessed by asking the patient to flex and extend his fingers and wrist. A complete motor block was defined as inability to move fingers voluntarily. The degree of tourniquet and hand pain was assessed using visual analogue scale (VAS). The duration of sensory and motor block after tourniquet release was determined by restoration of normal surface sensation and motor recovery as compared with the other sound limb. Any complication during surgery and after deflation of the tourniquet (such as nausea, vomiting, dyspnea, bradycardia, dizziness, or hypotension) was also recorded.

Statistical analysis

Data were expressed as mean ± SD unless otherwise indicated. Data were analyzed using fisher's exact t-tests and Mann Whitney test as appropriate. P-value <0.05 was considered statistically significant.

Results

Eighty patients were included in the study and were equally distributed among the two groups. There were no differences in the demographic data (age, weight, sex), duration of surgery and tourniquet time between both groups (Table 1). There was no significant difference in the onset of pinprick loss, touch loss and motor block between both groups (Table 2).

	Group C (n=40)	Group N (n=40)	P-value
Age (yr)	44.9 ± 13.3	45.3 ± 12.1	0.881
Sex (M/F)	32/8	28/12	0.439
Weight (kg)	76.4 ± 11.5	73.4 ± 13.1	0.281
ASA (I/II)	31/9	27/13	0.453
Surgical duration (min)	33.2 ± 8.4	35.9 ± 12.1	0.251
Tourniquet time (min)	47.7 ± 8.7	50.4 ± 12.1	0.254
Data were represented as mean ± SD unless otherwise indicated			

Table 1: Demographic and surgical data.

No significant differences were also observed in the pinprick, touch and motor block recovery after tourniquet deflation between both groups (Table 2).

At the time of admission in to the recovery room, we did not observe statistically significant difference in VAS score between both groups. Also no significant differences were observed between both groups as regards time to first analgesic request, the total dose of ketorolac used or the number of patients needing supplemental opioid (Table 3).

In addition, no significant differences in postoperative complications were observed between both groups (Table 4).

	Group (n=40)	C	Group (n=40)	N	P-value
Pinprick onset time (min)	7.3 ± 0.4		7.5 ± 0.4		0.128
Touch onset time (min)	10.2 ± 0.5		10.4 ± 0.7		0.235
Motor block onset time (min)	14.9 ± 1.5		15.1 ± 1.4		0.55
Pinprick recovery time (min)	4.0 ± 0.9		3.8 ± 1.0		0.287
Touch recovery time (min)	3.7 ± 1.2		3.4 ± 0.9		0.251
Motor block recovery time (min)	2.1 ± 0.6		1.9 ± 0.5		0.266
Data were represented as mean ± SD					

Table 2: Onset and recovery from sensory and motor block (min).

	Group (n=40)	C	Group (n=40)	N	P-value
VAS on admission to the recovery room	4.4 ± 1.4		4.1 ± 1.2		0.401
Time to 1st analgesic requirement (min)	25.3 ± 6.7		26.9 ± 7.3		0.334
Total ketorolac consumption(mg)	58.5 ± 23.5		61.5 ± 19.2		0.533
Patients in need of pethidine (No. (%))	5 (13%)		3 (8%)		0.712
Data were represented as mean ± SD and number (%)					

Table 3: VAS in the recovery room and the time of 1st analgesic requirement.

	Group C (n=40)	Group N (n=40)	P-value
Nausea	2 (5%)	5 (13%)	0.432
Vomiting	0 (0%)	2 (5%)	0.494
Dyspnea	0 (0%)	2 (5%)	0.494
Dizziness	5 (13%)	3 (8%)	0.712
Bradycardia	0 (0%)	1 (3%)	1
Hypotension	1 (3%)	2 (5%)	1

Table 4: Postoperative complications No. (%).

Discussion

The results of this study showed no significant differences between both groups in terms of gender, body weight, height, ASA status, type and duration of surgery and the tourniquet time. The study results also showed no statistically significant difference in both the onset of sensory and motor blocks; and the time to sensory and motor recovery in the two study groups.

Many studies on the analgesic efficacy of neostigmine in IVRA gave different results. Neostigmine has been used with different local anesthetic agents and in different doses. Turan et al. [10] in 2002 found that addition of 0.5 neostigmine to prilocaine causes shortened sensory and motor block onset, prolonged sensory and motor block recovery, improved quality of anesthesia and prolonged time to first analgesic request. The study by Turan et al. was in agreement with the results obtained by Marashi et al. [11] and Sethi et al. [12] in which 0.5 % lidocaine was used instead of prilocaine. Kang et al. [13] used ropivacaine and observed good outcome with 0.5 mg of neostigmine as an adjunct.

In contrary to our results, McCartney et al. [9] found no analgesic benefits of 1 mg neostigmine when added to 0.5% lidocaine. Kuyruklyildiz et al. also did not find analgesic effect of neostigmine when compared to control group [14].

Evidences for analgesic effects of neostigmine are more with its intrathecal and epidural administration. The increased concentration of Ach binds to the muscarinic receptors [15] placed in the dorsal horn cells, substantia gelatinosa and lamina III and V of the spinal cord [16] and nicotinic receptors [17-19] placed in the descending noradrenergic fibers [18], dorsal root ganglion [20] and in microganglia [19]. The presence of cholinergic activity seems to be an important condition for neostigmine analgesic effect [21,22] which could be reversed by muscarinic receptor antagonists [23]. Although Day et al. [24] suggests that Ach receptors exists in peripheral nerve endings, it seems that strong evidences are lacking for this mechanism in the periphery.

The mechanism of action of IVRA itself is still unclear [25], some authors suggest nerve trunk as the main site of action of local anesthetics [26,27], while others suggest peripheral sites to be the main site of action [28,29]. In both cases, the presence of blood-nerve barrier at the innermost layer of perineurium and at the endothelial microvasculature [30] with its highly specialized characteristics as "barrier forming cells" [31] may prevent the transport of neostigmine (a quaternary ammonium compound) to the site of action with the main local anesthetic.

In conclusion, we found that addition of 1 mg neostigmine to 0.5% lidocaine in IVRA has no anesthetic or analgesic effect and there is no increase in the incidence of complications. We did not find any biological fact that supports the use of neostigmine as adjuvant to local anesthetic agents in IVRA.

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