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# Atracurium with or without magnesium sulfate as an adjuvant to lidocaine for intravenous regional anesthesia in hand and forearm surgeries: A randomized controlled study

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***Abstract*---Background:** The use of adjuvant drugs in intravenous regional anesthesia [IVRA] for forearm and hand operations are used to elevate efficiency and quality of the block & decrease side effects. The optimal combination is achieved through ongoing experiments. **Objective:** To compare the outcome of Atracurium without or with Magnesium Sulfate added to lidocaine for intravenous regional anesthesia on analgesic efficacy after surgery throughout the 1st twenty-four hours, beginning and periods of recovery of motor and sensory blockades, and intraoperative analgesia. **Methods:** 75 cases designated for hand or forearm operation have been randomly assigned to three groups. Group A underwent three milligrams per kilogram of two percent lidocaine. Group B underwent three milligrams per kilogram of two percent lidocaine and two milligrams of atracurium. Group C underwent three milligrams per kilogram of lidocaine two percent with two milligrams of atracurium and ten milligrams per kilogram of magnesium sulfate. Every preparation has


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been diluted with saline to achieve a total volume of forty milliliters. Analgesia after surgery throughout the 1st twenty-four hours, the beginning and the periods of recovery of motor and sensory block, 1st analgesic request, and side effects of the study medications have been evaluated. **Results:** The VAS score after surgery was significantly reduced in group B & C about 12 h postoperatively. The period to 1st analgesia needs was significantly extended in B group in comparison with A group and the longest period has been documented in group C. The beginning periods of sensory and motor blockades have been reduced in group B and C in comparison with group A. Complete motor and sensory blockade happened in group B and C earlier in comparison with group A. **Conclusion:** The usage of magnesium sulfate as an alternative had a significantly superior analgesia after surgery, extended period of motor and sensory block, and previous beginning of action. Moreover, the usage of atracurium besides magnesium sulfate enhances the intravenous regional anesthesia quality.

***Keywords*---**Atracurium, Intravenous Regional Anesthesia, Magnesium Sulfate, hand and forearm surgerie.

## Introduction

Regional anesthesia represented the cornerstone of modern anesthetic clinical practice. It benefits from technological progresses; and have numerous benefits such as elevated satisfaction of the case, increased safety, and fast recovery [1].

IVRA is usually utilized for operation of upper limb persisting below an hour, being an efficient, simple, safe, and reliable method with minimal complications. Nevertheless, it isn't free from unwanted impacts such as local anesthetic toxicity, tolerance of tourniquet period is reduced, delayed beginning of action, poor muscle relaxation, quick beginning of pain following deflation [2].

Unfortunately, the quick dissipation of the block accompanied by subsequent pain following surgery is one of the restrictions of this method, as is 'tourniquet pain'. Many alternatives were tried in an effort to overcome these issues, such as tramadol, opioids, non-steroidal anti-inflammatory medications, potassium, muscle relaxants, dexmedetomidine, alkalinization with sodium bicarbonate, magnesium sulfate and nitroglycerine **[3].**

Lidocaine is the most common medication utilized in regional or local intravenous anesthesia. Nevertheless, it has numerous disadvantages, like a relatively reduced period of action [with restrictions of analgesia following surgery]. The usage of alternative might decrease such impacts and elevate it's potency **[4].**

Different neuromuscular blocking medications were utilized to enhance the operating conditions and decrease the dose of local anesthesia and probable systemic toxicity **[5].** The usage of Atracurium as an alternative in intravenous regional anesthesia is resulting from it's impact on muscle spindles; it decreases

central input from these structures, leading to muscle tone loss and regulate of voluntary motions with a reduction in nervous inputs to the brain **[6].** Moreover, blockade of muscle spindles stimulated by Atracurium can relieve muscle spasms and decrease pain both throughout and following operation **[4].**

Magnesium, which is known to be a 'Natural physiological calcium channel blocker,' is essential in the anti-nociception mechanism. Magnesium has endothelium derived nitric oxide stimulated vasodilation; consequently, it improves the activity of local anesthetic drugs and enhances anesthetic quality and extends motor and sensory blockade **[7].** The mechanism of the analgesic action of Mg is remains ambiguous, although a calcium channels disorder and the N-Methyl-D-aspartate (NMDA) receptor appears to have a significant role **[8].**
This research aimed to compare the outcome of Atracurium without or with magnesium sulfate added to lidocaine for intravenous regional anesthesia:

1- **Primary outcome:** Postoperative analgesic efficacy throughout the 1st twenty-four hours.
2- **Secondary outcomes:** (1) the beginning and periods of recovery of motor and sensory block. (2) Tourniquet pain. (3) Side effects (Lidocaine toxicity)**.**

**Patients and Methods**

This research has been performed at Al Azhar University Hospitals in Assiut following attaining approval from faculty of medicine ethics committee [approval number **MSc/AZ.AST. /14/181/1/2020]** and written informed consent from the cases during the duration from **January 2020** to **June 2020.**

**Inclusion Criteria:** 75 ASA grade I and II cases, aged between 21-40 years with body weight 60 - 70 kg, of either gender, designated for forearm or hand operation (e.g.: tendon repair, carpal tunnel, plating radius or ulna) were randomly selected.
**Exclusion Criteria:** Cases with sickle cell anemia, history of medication allergy, Raynaud's illness, myasthenia gravis, scleroderma, diabetes mellitus, heart illness, renal or liver deficiency or history of convulsions have been excluded from the research.
**Study design:** Prospective, randomized, double-blind controlled research.
**Grouping:**
All cases have been reserved fasting before surgery. The cases have been separated randomly into **3 Groups (A, B, C)** of **twenty-five patients each**, regarding computer generated table of random numbers.

- **Group A:** Patients underwent three milligrams per kilogram of two percent lidocaine.
- **Group B:** Patients received three milligrams per kilogram of two percent lidocaine and two milligrams of atracurium.
- **Group C:** Patients received three milligrams per kilogram of lidocaine two percent with two milligrams of atracurium and ten milligrams per kilogram of magnesium sulfate. (Every preparation have been diluted with saline to a total volume of forty milliliters)

**Preoperative assessment &Technique:**

All patients received premedication with IV midazolam (Midathetic 5mg/1ml-Amoun) at 0.05 mg/kg given 30 min preoperatively. In the surgery theatre, electrocardiogram, non-invasive arterial blood pressure and peripheral oxygen saturation following-up (by vamos-Drager-Germany monitor) has been started. 2 intravenous cannulas were positioned; 1 in a vein on hand dorsum to be operated (twenty-two gauge) and the other in the opposite hand. Double tourniquets were located on the upper arm of the hand to be operated. Arm has been increased for two minutes to drain blood vessels from blood before inflation of the tourniquet.

The upper (proximal) tourniquet has been finflated to a pressure of hundred millimeters of mercury above the systolic blood pressure of the case. The circulatory separation of the arm has been validated through examination the limb color, lack of radial pulse and loss of pulse oximeter tracing in the ipsilateral index finger. The anesthetic solution has been previously prepared through a detector and has been administered over a duration of ninety seconds through the cannula 22 in the hand that has been operated.

The beginning of sensory block has been evaluated through a pin prick conducted at one-min period in the dermatomal sensory distribution of the lateral and medial ante brachial cutaneous, ulnar, radial and median nerves. (0 = sharp, 1 = touch only, and 2 = can't feel touch). Score two was considered to indicate the beginning of complete sensory blockade. The beginning period of sensory block has been documented as duration elapsed from injection of medication to sensory block attained in every dermatome.

The beginning of motor block has been evaluated through asking the case to flex and prolong his or her fingers and wrist. Following of motor block has been evaluated via **Modified Bromage Score** (0 = normal motor function, 1 = decreased motor strength but may move fingers, and 2 = complete motor block). Complete motor block has been recorded when no voluntary movement was possible.

When case feels discomfort at the proximal tourniquet location, the distal tourniquet has been inflated to the same pressure and proximal one has been deflated. Then let the surgeon started the operation.

Beginning period of upper tourniquet pain has been documented. Evaluation of tourniquet pain and analgesic level during surgery has been evaluated through **Visual Analogue Scale** of zero to ten every 20 minutes (0 = "no pain" and 10 = "Worst pain imaginable"). The tourniquet wasn't deflated before thirty minutes and wasn't kept inflated for above 2h.

**- At the end of surgery,** the tourniquet has been deflated through a cyclic deflation method and documenting this: Sensory block period of recovery, Motor block period of recovery & visual analogue scale (post-operative VAS) was documented at 0, 15 minutes, 1, 6, 12, and 24h. The period to 1st analgesic need was documented (The duration from the release of the tourniquet to the initial case request for analgesia).

- Nalbuphine four milligrams was administered intravenously for rescue analgesia when visual analogue scale scores not less than four at any time in 1st twenty-four hours after sergury**)**.
**-Patient satisfaction:** Case satisfaction score was implicit as five = very satisfied, four = satisfied, three = neutral, two = dissatisfied, and one = very dissatisfied.

**Sample size calculation:**

This study has been depended on an earlier research [9]. Eoi info statcalac has been utilized to estimate the size of the sample through regarding the following assumptions: ninety-five percent 2 sided confidence level, with a power of eighty percent & alpha errors of five percent. The final maximum size of the sample was 75 to assume any drop out patients throughout monitor, 25 patients in every group.

**Statistical analysis:**

All data was collected and cleaned by Excel program using SPSS version 20.0. Results was given as mean ± SD. Demographic data was compared with ANOVA (analysis of variance) Statistical significance has been set at P-value below 0.05 percent.

**Results**

In this randomized, prospective, double blind controlled research, 90 cases have been evaluated for eligibility. Ten cases didn't fulfill the inclusion criteria, five cases rejected to participate, and the rest of the 75 patients were enrolled randomly in the research, with 25 cases in every group. These patients completed the research and have been analyzed finally.

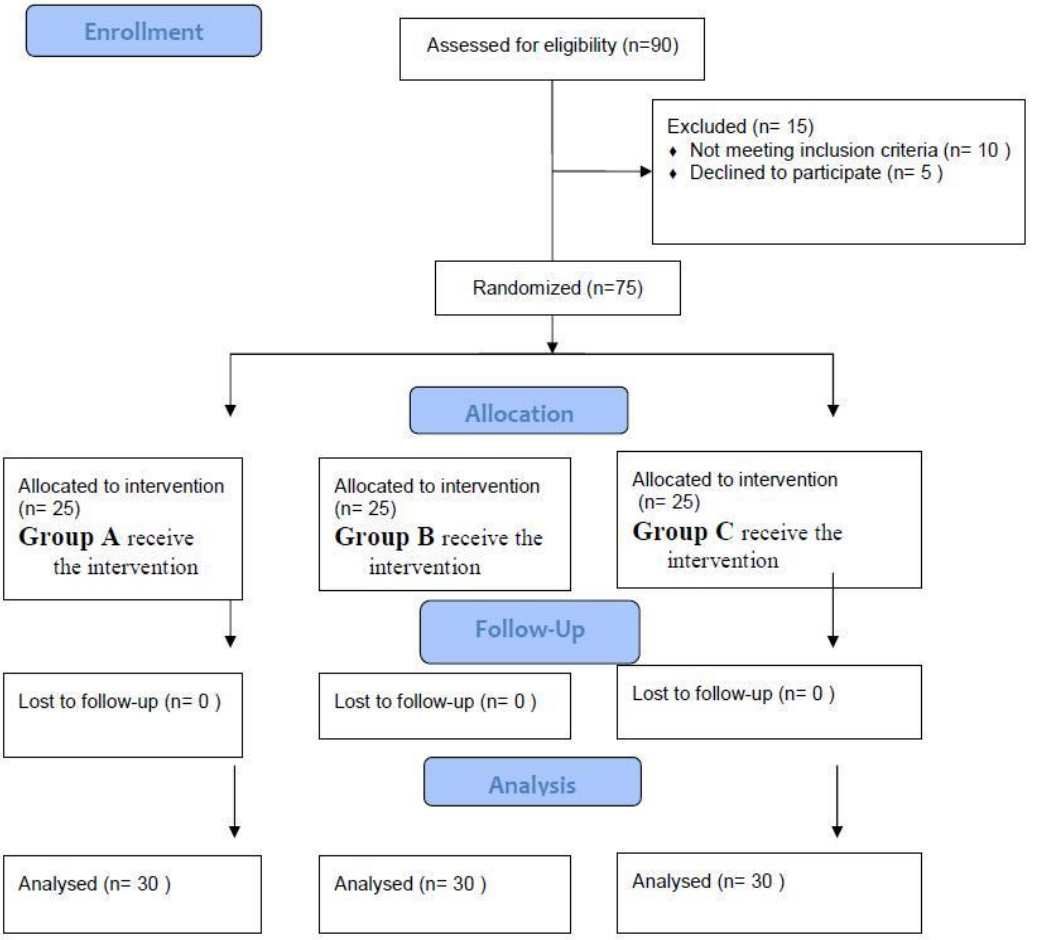


Fig. (1): CONSORT flow chart of the enrolled patients

**A- Patient characteristics:**

Patient gender, age, weight, ASA, operation type, operation period and tourniquet period were similar in each the 3 groups and there a statistically insignificant variance has been observed between the three groups.

Table (1): Comparative analysis between examined groups as regards Patient characteristics:

| | Group A | Group B | Group C | P value |
|---|---|---|---|---|
| **Age (year)** | 30.6 ± 6.7 | 28.9 ± 5.6 | 30.4 ± 5.4 | 0.54 |
| **Gender Male/female** | 17/8 | 21/4 | 20/5 | 0.24 |
| **ASA 1/I/II** | 19/6 | 17/8 | 20/5 | 0.415 |
| **Weight(kg)** | 71.8 ±9.1 | 69.5 ± 6.3 | 70.8 ± 4.9 | 0.518 |
| **Duration of** | 64.8 ±11.1 | 62.5 ± 12.5 | 69.8 ± 9.8 | 0.073 |

| | Group A | Group B | Group C | P value |
|---|---|---|---|---|
| **surgery(minutes)** | | | | |
| **Tourniquet time (minutes)** | 51.2 ± 7.4 | 53.2 ± 4.2 | 51.1 ± 4.2 | 0.302 |
| **Type of surgery:** | | | | |
| - **Carpal tunnel** | 13 | 10 | 12 | 0.890 |
| - **Tendon repair** | 7 | 8 | 6 | |
| - **Plating radius or ulna** | 5 | 7 | 7 | |

**B- Sensory and Motor block:**

**Beginning periods of motor and sensory blockades intraoperative** were **reduced** in the **B** group (4.4±1.9 min and 6±1.9 min) and in the **C** group (4.4±1.1 and 4.6±0.8 min) than in the **A** group (6.8±2.2 and 11.6±3.2 min). (Table 3), and **complete motor and sensory block** occur in group **C** and **B** earlier compare to group **A**. A statistically significant variance has been observed (p-value below 0.05).

**Table (2):** Comparative analysis between examined groups concerning motor and sensory block

| | Group A | Group B | Group C | P value |
|---|---|---|---|---|
| **Onset of sensory block (minutes)** | 6.8 ± 2.2 | 4.4 ± 1.9 | 4.4 ± 1.1 | 0.001 |
| **Complete of sensory block (minutes)** | 11.1 ± 2.5 | 9.9 ±2.4 | 10.2 ± 1.2 | 0.174 |
| **Onset of motor block (minutes)** | 11.6 ± 3.2 | 6 ± 1.9 | 4.6 ± 0.8 | 0.001 |
| **Complete of motor block (minutes)** | 18.1 ± 3.7 | 11.5 ±2.5 | 11.1 ± 1.8 | 0.001 |

**C- Recovery of sensory and motor blockades :**

Beginning of recovery of motor and sensory blockades postoperative were **extended** in the **B** group (9.9±1.9 min and 9.1±2.6 min) and in the **C** group (9.1±2.1and 9.8±1.9 min) than in the **A** group (7.9±3 and 3.5±1.6 min). (Table 3). A statistically significant variance has been observed.

**Table (3):** Comparative analysis between examined groups concerning beginning of recovery of motor and sensory blockades

| | Group A | Group B | Group C | P value |
|---|---|---|---|---|
| **Sensory block recovery time (minutes)** | 7.9 ± 3 | 9.9 ± 1.9 | 9.1 ±2.1 | 0.042 |
| **Motor block recovery time (minutes)** | 3.5 ±1.6 | 9.1 ± 2.6 | 9.8 ±1.9 | 0.001 |

*Statistically significant variance (p-value below 0.05)

**D- First Time Analgesia:**

Period to 1st analgesic need was significantly **extended** in the **B** group (37.1±12.2 min) than in the **A** group (24.4±13.7 min), and **the longest time** in **C** group (90.5±30.5 minutes). A **statistically significant** variance between the three groups. Table (4).

**Table (4):** Comparative analysis between examined groups concerning first time analgesia information

| | Group A | Group B | Group C | P value |
|---|---|---|---|---|
| **First time analgesia** | 24.4±13.7 | 37.1±12.2 | 90.5±30.5 | <0.001 |

**E- Visual Analogue Scale (VAS):**

Visual analogue scale score was lower in group B and C compared to group A. A statistically significant variance has been observed (p-value below 0.01) between examined groups concerning intra-operative and post-operative VAS (Figs. 2 & 3).

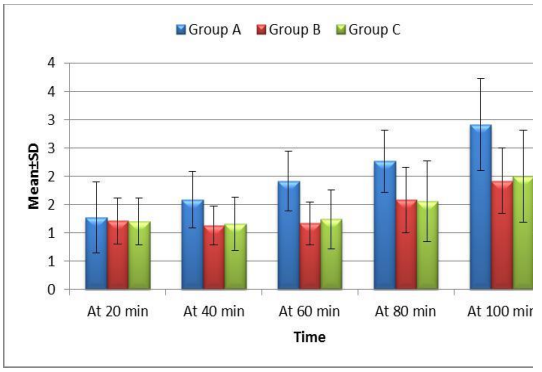


**Fig. (2):** Intra operative VAS.

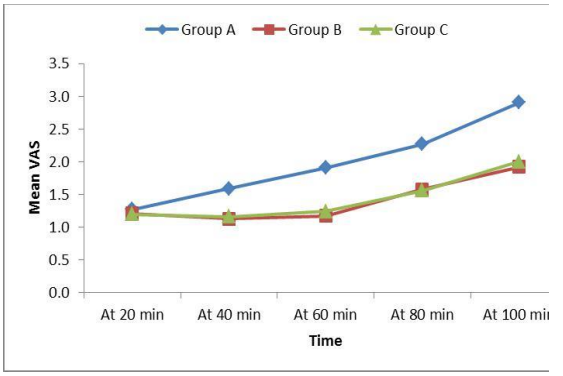


**Fig. (3):** Postoperative VAS.

**F- Side Effects**

Oral numbness happened in 2 cases in group A and in 1 case in group C, and no patients suffered from oral numbness in group B. Dizziness happened in one case in group A, with no noted cases of dizziness in the other groups

**Discussion**

The fundamental concept of the Bier block is to exsanguinate the extremity, applying an arterial tourniquet to separate it from circulation, and inject local anesthetic into the extremities venous system, stimulating anesthesia **[10]**.

The results of this study showed that period to 1st analgesia request was significantly extended in group B in comparison with group A and the longest period has been documented in group C. The beginning period of sensory blockade has been reduced in group B and C paralleled to group A. Motor block beginning time was shorter in group C, then group B and A; a significant variance

has been observed between all study groups. Complete motor and sensory block happened in group B and C earlier in comparison with group A. The beginning of recovery of motor and sensory blockades postoperative was extended in group B and C in comparison with group A. The Visual Analogue Scale score after surgery was significantly diminished in group B and C paralleled to group A up to twelve hours after surgery; insignificant variance was observed among the groups 24 h after the surgery.

VAS for pain as regards intra-operative VAS and post-operative VAS in group **B** was reduced in comparison with group **A** as supported also by **Hassan and Faez [13].**

**Tramer and colleagues [17]** shown that cases receiving Mg as an adjuvant in analgesia after surgery, required less morphine, had reduced distresses and achieved superior sleep quality through the 1st forty-eight hours compared to those administering morphine alone.

**Mirkheshti and his colleagues [11]** proposed that the addition of magnesium to lidocaine (three milligrams per kilogram of lidocaine with one gram MgSO4) throughout upper extremity orthopedic operation with intravenous regional anesthesia significantly decreases the duration among the medication administration and the beginning of blockage is significantly deceased. Furthermore, this medication mixture elevated block length of intravenous regional anesthesia, while the giving of paracetamol didn't exert this impact.

**Tramer and Glynn [17]** used 500 mg MgSO4 to treat chronic limb pain with intravenous regional anesthesia and demonstrared that adding magnesium to lidocaine increased the block quality and prolonged the analgesia. According to another study, the response times for sensory and motor blockages in magnesium sulfate were statistically shorter.

**Choyce and Peng [12]** stated that the usage of NSAIDs or clonidine as assistants to improve analgesia after surgery in IVRA and muscle relaxants enhance motor block during surgery and assist fracture decrease.

Another study by **Hassan and Faez** found that a mixture of Atracurium and ketamine added to lidocaine led to quick beginning of sensory and motor block, reduced Visual Analogue Scale scores for pain, and fewer side effects of Bier's block accompany lidocaine alone **[13].** In agreement with this, we recorded lower intraoperative VAS and postoperative VAS in group B in comparison with group A.

**Flamer and Peng [14]** stated in their review that the combination of muscle relaxants (mivacurium, pancuronium, cisatracuriumA tracurium,) and fentanyl can yield the same value of IVRA with a 50% reduce in the local anesthetic dose, but with a potentially slower beginning of sensory block. Furthermore, **Esmaoglu et al. [21]** documented that, the addition of cisatracurium to lignocaine in intravenous regional anesthesia reduced the motor and sensory block beginning periods, enhanced quality of the anesthetic, and reduced analgesic needs without resulting in clinical side effects.

The values of postoperative VAS score were reduced in **C** group in comparison with **A** group as supported by **Turan et al. (7).** Injection period of 1st dose of analgesic (minutes). A statistically significant variance has been observed in injection period of 1st dose of analgesic in all the two groups **(B, C)** in comparison with the control group **(A).** Our outcomes are agreement with the outcomes of **Turan et al. (7)** who observed that the period to 1st analgesic request following surgery in magnesium sulphate group was statistically significant.

**Wahba and Tammam [15]** studied three groups of twenty cases each: The R group, which underwent intravenous regional anesthesia with ropivacaine 0.2%; the RM group, which underwent intravenous regional anesthesia utilizing ropivacaine 0.2% and MgSO4 ten milligrams per kilogram; and the RMV group, which underwent intravenous regional utilizing ropivacaine 0.2 percent and a single systemic intravenous dose of MgSO4 thirty ten milligrams per kilogram. They found that the addition of magnesium to ropivacaine in the IVRA increased the block quality and decreased tourniquet discomfort, and systemic administration of magnesium led to decreased morphine consumption and postoperative pain.

**Bansal et al. [16]** concluded that adding all magnesium sulfate and nitroglycerin to lidocaine in intravenous regional anesthesia led to early beginning of sensory blockage and sustained analgesia after surgery, with no side effects. These outcomes are in agreement with earlier researches of **Gorgias et al. [18], Honarmand et al. [19], and Hegazy et al. [20],** observed no adverse impacts happened throughout intravenous regional anesthesia with the usage of adjuvants.

**Limitations:** The size of the sample was small.

**Recommendations**

Further researches with various doses of magnesium sulfate and Atracurium will aid determine the sufficient dose for the best clinical and postoperative analgesia. Other studies with different combinations should be tried.

**Conclusion**

The usage of magnesium sulfate as an alteration had significantly superior analgesic impacts after surgery, extended period of motor and sensory blockade, and earlier beginning of action. Furthermore, atracurium, besides magnesium sulfate, enhances the IVRA quality**.**

**Declarations:** All authors contributed equally to this research. The authors of this manuscript clarify no conflict of interests.

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